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MALIGNANT HYPERTENSION

REPORT OF CASE TREATED BY BILATERAL SECTION OF ANTERIOR SPINAL NERVE ROOTS FROM THE SIXTH THORACIC TO THE SECOND LUMBAR, INCLUSIVE

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The maintained vasodilatation [1] produced by sympathectomy in the treatment of certain types of peripheral vascular diseases has stimulated us to investigate surgical procedures on the sympathetic and central nervous systems with the hope that severe forms of hypertension of young people might be controlled.

REASONS FOR TRYING SURGICAL MEASURES

In 1923 Brüning [2] suggested sympathectomy for the possible control of hypertension.

In the treatment of vasospastic lesions of arteries of the extremities, by sympathetic ganglionectomy and trunk resection, we have observed that the blood flow has been increased as measured in degrees of increased elimination of heat. The measurement of retinal arteries and veins by an ophthalmoscopic micrometer before and after cervicothoracic ganglionectomy shows that the caliber of these vessels has been increased by the sympathectomy [3] from a third to a half the preoperative size. Therefore we dared to postulate that it might be possible to interrupt sufficient vasoconstrictor fibers to alter the arterial tension and to prevent the sudden and paroxysmal rises, which may produce arterial rupture in the advanced stages of the disease.

We were aware that many factors are involved in the production of hypertension, but since medical measures had not offered the solution to the problem, we believed that we were justified in proceeding with our surgical investigations. Whether or not our hypothesis might prove true, we also had to take into consideration the effects of sympathectomy on the function of organs deprived of their innervation in our attempt to paralyze the vasomotor control over a large vascular bed.

On interrupting the nerves that are involved in vasomotor control, we had hoped that hypertonus of the sympathectomized arteries might be reduced and also that additional vasodilatation might take place in the same group of arteries. That is, we hoped to prepare a vascular reservoir for emergency, and to avoid the sudden high rises of arterial tension.

We chose to alter the vasomotor control of arteries below the diaphragm, believing that injurious effects would not result and that the celiac and mesenteric arteries would lend themselves best to vasodilatation. It was apparent that periarterial sympathectomy would not be practical, and therefore we directed our first attack on the sympathetic rami communicantes, ganglions and trunks but later sectioned the anterior spinal roots bilaterally, from the sixth thoracic to the second lumbar inclusive, in order (1) to include all sympathetic fibers leaving by or returning through the anterior roots, thus interrupting the thoracicolumbar sympathetic outflow below the fifth thoracic segment and (2) to paralyze the abdominal muscles.

By the latter procedure we hoped (1) to sympathectomize sufficient arteries to modify arterial responses, (2) thoroughly to sympathectomize the suprarenal glands and (3) to remove the effects of intra-abdominal tension.

SURGICAL MEASURES TRIED

In 1925 Rowntree and one of us [4] reported a case of malignant hypertension in which treatment was by bilateral sympathetic lumbar ganglionectomy and trunk resection, which included the second, third and fourth lumbar sympathetic ganglions and the intervening trunks. The results on the blood pressure and ultimate outcome were not significant. It was apparent that the operation did not denervate sufficient arteries to change the systemic arterial pressure and that a more extensive operation was needed. One of us (Adson) suggested and performed an extensive rhizotomy in order to include all sympathetic innervation below the diaphragm and to include the motor innervation of the abdominal muscles.

Aug. 6, 1930, a patient with malignant hypertension was subjected to bilateral section of the anterior and posterior nerve roots from the sixth thoracic to the second lumbar, inclusive, through an approach afforded by laminectomy. The reasons for suggesting this procedure were that (1) the blood pressure always dropped and the vasopressor reactions were inhibited following spinal anesthesia; (2) the patient under consideration presented vasodilatation of the arteries of the hand and fingers following block anesthesia by procaine of the cervicothoracic ganglions, in spite of organic hyper-

From the Section on Neurologic Surgery and the Division of Medicine, the Mayo Clinic.

1. Brown, G. E., and Adson, A. W.: Calorimetric Studies of the Extremities Following Lumbar Sympathetic Ramisection and Ganglionectomy, Am. J. M. Sc. **170**: 232-240 (Aug.) 1925.

2. Brüning, Fritz: Die operative Behandlung der Angina Pectoris durch Exstirpation des Hals-Brustsympathicus und Bemerkungen über die operative Behandlung der abnormen Blutdrucksteigerung, Klin. Wchnschr. **2**: 777-780 (April 23) 1923.

3. Craig, W. McK., and Brown, G. E.: Resection of the Splanchnic Nerves in Cases of Hypertension, Proc. Staff Meet., Mayo Clin. **8**: 373-376 (June 14) 1933.

4. Rowntree, L. G., and Adson, A. W.: Bilateral Lumbar Sympathetic Neurectomy in the Treatment of Malignant Hypertension: Report of Case, J. A. M. A. **85**: 959-961 (Sept. 26) 1925.

trophy of the medial coats of the arterioles, and (3) this patient exhibited sharp hypertensive crises, with subjective symptoms and with inordinate increases in the blood pressure, which should theoretically be inhibited by denervating the splanchnic circulation.

In view of the progressive character of the hypertension and the short expectancy of life, the patient elected the operation even though informed that the muscles of the abdomen and lower costal muscles would be inactive, and that it would be necessary for him to wear an abdominal support. These facts previously had been learned from a case in which extensive rhizotomy had been performed by one of us (Adson) for gastric crisis of tabes. In the case in which operation was performed Aug. 6, 1930, ether anesthesia was used. During the early part of the operation the systolic blood pressure often rose higher than 200 mm. of mercury, but at the close of the operation it had dropped to 100 mm. The diastolic pressure dropped from 120 to 90 mm. The

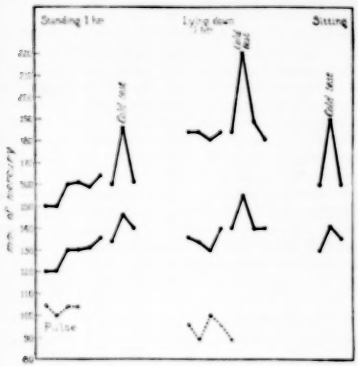

Fig. 1.—Blood pressure and response to the cold test with changes in posture.

operation otherwise was uneventful except that it required considerable time to complete, as every precaution was employed to insure hemostasis; in spite of this, postoperative bleeding developed and necessitated opening of the wound. The blood pressure one month after operation varied from 140 to 160 systolic and from 80 to 110 diastolic. The headaches and crises of paroxysmal hypertension had disappeared. One year later this control was still effective. Changes in the spinal cord developed following the hemorrhage, and it has been difficult to continue with controlled physiologic studies, which explains the absence of previous reports.

Subsequently Pieri,[5] and later Craig,[6] developed a procedure that permitted resection of the major and minor splanchnic nerves and the first lumbar ganglion. This procedure was divided into two stages. In the first stage the nerves on the one side were resected and in the second stage those on the opposite side. The procedure did not include the rami to the second lumbar ganglions; therefore the suprarenal glands were not completely sympathectomized. The results were variable, and in the severe type of hypertension not as much was accomplished as was hoped for.

The reduction and inhibition of the crises of blood pressure effected in the initial case in which rhizotomy was performed encouraged us to employ extensive rhizotomy again, with the view of controlling the severe form of hypertension.

REPORT OF CASE

A woman, aged 29, was first seen at the clinic in 1923, at which time she complained of headaches and high blood pressure of eighteen months' known duration. On admission the blood pressure, in millimeters of mercury, was 228 systolic and 156 diastolic. There was no evidence of renal disease. The retinal arterioles were constricted. The hourly readings of blood pressures taken under resting conditions varied from 150 to 200 systolic, and from 100 to 150 diastolic. The patient's diet was restricted, following which the headaches were relieved.

The patient returned to the clinic in 1933 because of marked fatigue, headaches, palpitation and dyspnea. The headaches usually were of the frontal type, but at times they were occipital on her arising in the morning. The blood pressure on admission was 240 systolic and 165 diastolic; the pulse rate was 120 beats per minute, and the heart was enlarged to grade 3. There was a soft systolic murmur in the mitral area. The retinal arteries were sclerosed, graded 2, with angiospasm; new and absorbing hemorrhages, and a few cotton-wool exudates were present in each eye; these are the features of retinitis of severe hypertension of group 3, the borderline malignant form of hypertension.[7] Hourly readings disclosed a variation in systolic blood pressure of from 180 to 230 mm. of mercury, and in diastolic pressure of from 110 to 160 mm. With the cold pressor test the blood pressure was increased to 280 systolic and 180 diastolic. The value for urea was 28 mg. per hundred cubic centimeters of blood. The value for sulphates was 5 mg. per hundred cubic centimeters of serum. Albumin was not present in the urine, but there were occasional casts. The electrocardiogram disclosed a diphasic T wave in derivation III. The basal metabolic rate was + 23. The diagnosis was essential, early malignant type of hypertension without renal insufficiency.

Operation was performed, Oct. 10, 1933, under ether anesthesia, and was not attended with any unusual incident. It included bilateral section of anterior nerve roots from the sixth thoracic to the second lumbar, inclusive. The posterior roots were not sectioned, and the second lumbar anterior root on the right was found to be incompletely sectioned. The purpose of the operation in this case was to interrupt all thoracicolumbar sympathetic fibers below the sixth thoracic segment, thus paralyzing vasoconstrictor nerves below that level, including the sympathetic supply to the suprarenal glands and, in addition, paralyzing the abdominal muscles further to reduce intra-abdominal tension. This was accomplished, with the possible exception of the right second lumbar root. During the early part of the operation the blood pressure rose to 250 mm. systolic and 178 diastolic. Ether anesthesia undoubtedly was responsible for the rise, but the subsequent marked fall to 80 systolic and 50 diastolic could scarcely be accounted for by the effects of shock, for there was practically no loss of blood during the laminectomy. From our previous experience, extreme care was taken to avoid injury to the small arteries and veins on the roots during the dissection and resection of the anterior roots, and to insure hemostasis. Postoperative convalescence was uneventful. The wound healed by primary union, and no complications arose. The patient had no disturbance of micturition or of defecation. The motor powers and sensation of the extremities remained normal. The muscles of the abdomen were relaxed, but since the patient was of asthenic type there was no sagging or bulging. The patient did complain of a slight drawing sensation

5. Pieri, Gino: La resezione dei nervi splancnici, Ann. ital. de chir. **6**: 678-684 (July) 1927.

6. Hines, E. A., Jr., and Brown, G. E.: A Standard Test for Measuring the Variability of Blood Pressure: Its Significance as an Index of the Prehypertensive State, Ann. Int. Med. **7**: 209-217 (Aug.) 1933.

7. Wagener, H. P.; Barker, N. W., and Burke, C. F.: Acute Angiospastic Retinitis: Occurrence in Cases of Severe Hypertensive and Renal Disease, Am. J. M. Sc. **185**: 517-528 (April) 1933.

in the region of the left loin the first three or four days when she was up in a chair, but this disappeared when an abdominal support was applied. The patient was dismissed from the hospital at the end of four weeks but remained under observation for another week in order that physiologic studies might be made.

SUBSEQUENT OBSERVATIONS

Hourly readings of the blood pressures were made the day following operation. The mean levels were 100 mm. of mercury systolic and 70 mm. diastolic. The second day the blood pressure had increased to 170 systolic and 130 diastolic. It remained at approximately this level when the patient was recumbent. Thirty-one days after operation the mean levels of blood pressure, with the patient recumbent, were 180 systolic and 125 diastolic. The range was from 155 to 195 systolic and from 100 to 150 diastolic. The response to cold when the patient was recumbent raised the blood pressure to 220 systolic and to 155 diastolic. At this time the patient had resumed her normal activity.

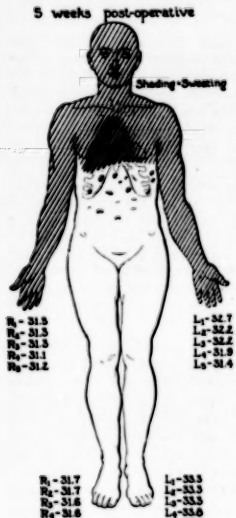

Fig. 2.—Sweating and surface temperatures of fingers and toes thirty-five days after operation.

Postural Effects on the Blood Pressure on the Thirtieth Day After Operation.—When the patient was sitting, the blood pressure on repeated tests varied from 160 to 170 systolic, and the diastolic pressure remained at approximately 130 (fig. 1). The response to cold with the patient sitting gave a maximal value of 190 systolic and 142 diastolic. With the patient standing, the blood pressure varied from 150 to 162 systolic and from 120 to 135 diastolic. The response to cold, when the patient was standing, gave a maximal increase to 186 systolic and 145 diastolic. With the sharp drop in the systolic blood pressure, when the patient was standing, the patient did not experience any subjective symptoms. The pulse rate increased twenty beats per minute.

Passive changes of posture on an adjustable table gave the following readings: recumbent, 190 systolic, 140 diastolic; head down at an angle of 90 degrees, 200 systolic, 142 diastolic; head up at an angle of 90 degrees, 168 systolic, 120 diastolic.

Sweating.—Thirty-five days after operation, demarcation of the sweating zone was determined by placing the patient in a sweating cabinet. Cobalt blue test papers were used to detect the nonvisible degrees of perspiration. No visible sweating was found below the level of the epigastric notch in front or of the angle of the scapulae in the back. Faint degrees of sweating were found in isolated areas on the skin of the upper part of the abdomen (fig. 2).

Surface Temperatures of Lower Extremities.—The temperature of the skin of the right and left toes was significantly different. The average for all digits of the right foot was 31.7 C., and that for the digits of the left foot, 33.7 C. The difference in surface temperature was noted both objectively and subjectively and is probably explained by the incomplete division of the second right lumbar anterior root.

Renal Function.—The patient was given 200 cc. of water, and the bladder was emptied at the end of one hour. Excretion of water was 60 per cent when the patient was recumbent and 10 per cent when the patient was standing. There was no difference in the amount of phenolsulphonphthalein excreted whether the patient was standing or recumbent.

Retinal Arteries.—The retinal arteries were still definitely narrowed. Sclerosis was present in most of the vessels. There was one definite cotton-wool exudate in the left retina. Retinitis was much less active than when the patient was admitted.

Untoward Effects Following Operation.—Some weakness of the abdominal muscles was noticed by the patient when she stood. She had some difficulty in assuming the sitting position. There was no objective bulging of the rectus abdominis muscles. It was found that the drop in the blood pressure when the patient stood was less marked after a snug abdominal support had been applied (fig. 3).

COMMENT

The patient whose case is here reported in detail had a severe, progressive form of essential hypertension. Organic changes in the retinal arterioles, and active retinitis were present. The length of life in this type of case after such changes have been noted, as has been shown by Keith,[8] is usually less than three years. One month following resection of the anterior spinal

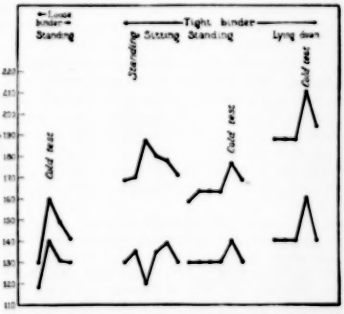

Fig. 3.—Drop in blood pressure less with abdominal support. The pressor reaction to cold is increased.

nerve roots there was a definite drop in blood pressure, more marked in the systolic than the diastolic, when the patient was recumbent, but this lowering of pressure was accentuated by the upright posture. In this position there was, for this patient, relative hypotension. It is obvious that restoration of this patient's diastolic blood pressure to normal levels would be impossible

8. Keith, N. M.; Barker, N. W., and Kernohan, J. W.: Histologic Studies of the Arterioles in Various Types of Hypertension, Tr. A. Am. Physicians **46**: 66-68, 1931.

because of the structural hypertrophy of the arterioles. While this patient is active and up and about, the range and variation of her blood pressure are those of a moderate degree of hypertension, and during this active period the overload on the heart and other organs is materially diminished. It is probable that this decrease in the pressures during a larger portion of the period of twenty-four hours should be of great benefit. The argument often advanced, that high levels of blood pressure of patients with hypertension should be maintained for the kidneys to function adequately, is not demonstrated in this case. The activity of the heart and kidneys is well maintained, with a drop of 80 mm. of mercury in systolic pressure. The excretion of water was not materially modified but was merely delayed, and this was only an exaggeration of what occurs among normal subjects when they are recumbent. A change in the size of the arterioles of the retina could not be demonstrated in this short period, but decrease in the activity of the retinitis was noted. The effects of the operation on the pressor reactions to cold were of interest. It has been shown that this pressor response is comparable to the effects of psychic and emotional stimulation on the blood pressure. It constitutes an accurate measuring rod to determine effects of treatment on variability of blood pressure. Following operation there was a significant decrease in the maximal rise in blood pressure. This was more marked when the patient was upright; namely, there was a decrease of 100 mm. of mercury in the response of the systolic pressure. This effect was further confirmed by the postoperative hourly readings of blood pressure taken under various forms of mental and physical activity. Denervation of the vessels below the diaphragm of the patient did not completely inhibit the pressor responses to cold; this may be the effect of the vasoconstrictor response of the arteries of the upper part of the body. The effects of the operation on the sweat and vasomotor fibers indicated that almost complete degeneration of the sweat fibers had taken place below the level of the episternal notch. It is probable that the depressor effects of this operation were the result of two factors: (1) loss of vasomotor control of the splanchnic and peripheral arteries below the diaphragm, and (2) lowering of intra-abdominal pressure by paralyzing the abdominal muscles.

The favorable results of this operation in so severe a form of hypertension are most encouraging, and its further use for younger patients with severe progressive forms of essential hypertension seems justified.

Wheals.—We know that an urticarial wheal can be produced in normal persons by the injection of histamine, morphine and innumerable other substances and also by localized mechanical, thermal or electrical injury. We also know that in patients with serum sickness, hay fever, asthma and eczema the intradermal injection of the substances to which they are sensitized produces a wheal although these substances have no such effect on normal skin. The serum of allergic subjects will often locally sensitize the skin of normal persons so that it in turn will react to subsequent injection of the allergen or, in some instances, to absorption of the allergen after it is swallowed. The investigations of Philippson, Lewis, Blackley, Prausnitz and Küstner, Walzer and others have established these facts and added greatly to our knowledge of the pathogenesis of wheals. There remains, however, a gap between our understanding of the mechanism of wheal formation and our information as to the causes of the general eruptions of wheals which we refer to as urticaria. Urticaria is a symptom of many diseases.—Hopkins, J. G., and Kesten, B. M.: Urticaria.—Etiologic Observations, *Arch. Dermat. & Syph.* **29**:358 (March) 1934.

SUBTOTAL BILATERAL SUPRARENALECTOMY FOR HYPERSUPRARENALISM

(ESSENTIAL HYPERTENSION)

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Down to the present time, a study of the vasoregulatory mechanism would indicate the futility of an attempt to pick out and burden one single link of the chain and place the responsibility on this for alterations of the whole system. This does not mean, however, that a better understanding of the whole problem could not be arrived at if one of these links was studied with particular care.

The heart and the peripheral vessel system must decide the issue. Both are under the regulation of nervous influences, which either act directly on the cardiac and vascular musculature and on the contractile elements of the capillary walls or are brought to bear on them indirectly through the mediation of hormones. The part played by the blood electrolytes in determining the effect of the hormone concentration is also a deciding factor.

In our studies, this being a preliminary report, an attempt is made to cut down the suprarenal hormone concentration of the blood, confining our observations at present to the so-called essential hypertension group. The treatment of essential hypertension, associated with little or no arteriosclerosis and no kidney destruction, has presented apparently insuperable difficulties to the internist. Little of permanent value has been accomplished in these cases, and they usually go on to a fatal termination. We have felt for some time that the picture is one of an endocrine dyscrasia and that the responsible glands are the suprarenals. We know that the secretion of the medulla of the normal suprarenal raises the blood pressure, and it is reasonable to assume that the increased secretion contingent on an abnormal suprarenal might give the symptom of so-called essential hypertension.

Assuming that essential hypertension is due to excessive secretion of epinephrine by hyperplastic suprarenals, comparable to the excessive secretion of thyroxine in hyperplastic thyroids, we have attempted to reduce the secretion by subtotal suprarenalectomy in a number of cases, the results of which will be shown in this paper.

Of all the endocrine glands, the one about which the most is known is the thyroid. This is, in fact, due to its accessible position. While we would not imply that the last word has been said regarding the thyroid, it is well known that in certain pathologic states there is an increased secretion of its normal thyroxine, and it is known that the resulting symptomatology, with its tachycardia, tremor, vasodilatation, loss of weight, increased basal metabolic rate and the like is due to the increased secretion circulating in the blood stream. It is also known that the disturbance of the thyroid gland itself which causes the hypersecretion is one of hyperplasia. What causes the hyperplasia of the thyroid is as yet only a matter of conjecture, but there is evidence

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supporting the view that the vegetative nervous system plays an important rôle in it.

The suprarenal, because of the large network of nerve fibers connected with its capsule, has been called the brain of the vegetative nervous system. It seems logical, therefore, to find an analogy between the overactivity of the thyroid, due to sympathetic stimulation causing hyperthyroidism, and the overactivity of the suprarenals, due to sympathetic stimulation causing hypersuprarenalism. If this analogy is valid, partial suprarenalectomy should give results in hypertension comparable to those obtained from thyroidectomy for hyperthyroidism.

In all our cases of hyperthyroidism in which an operation has been performed and which later exhibited recurrent symptoms of hyperthyroidism, we have been able to show an increase in the remaining hyperplastic tissues and have accordingly relieved our patient by again lessening the amount of the remaining tissue. In one case, partial thyroidectomy was performed no less than five times, with eventual complete relief of symptoms and restoration of a normal basal metabolic rate.

Crile [1] has felt that even in these cases the suprarenal has been the activating influence and reports relief of symptoms through severing of the afferent nerves of the suprarenal gland. We ourselves performed suprarenal denervation in six cases of neurocirculatory asthenia with very indifferent results. In this disease there is almost always a normal or slightly lowered blood pressure, both systolic and diastolic. We believe, however, that in cases of hyperthyroidism the attack should be made on the thyroid itself, whenever possible. But even in pure hypersuprarenalism, denervation as performed by Crile does not seem to us to be sufficient, probably because a hyperplasia of the gland already exists, just as cervical sympathectomy was unsatisfactory in hyperthyroidism, and for the same reason.

Pende's [2] experimental denervation of a suprarenal gland in a kitten from which the other suprarenal had been removed two months previously resulted, six months later, in a well maintained cortex and a completely atrophied medulla; but here there was no question of an existent hyperplasia, the organ being practically normal when denervation was done.

REPORTS OF SUPRARENALECTOMY IN THE LITERATURE

A glance over the literature reveals but few cases in which the attempt has been made to reduce essential hypertension by partial suprarenalectomy.

Galatà [3] and Antonucci in 1929 removed one entire suprarenal from a woman in a desperate condition with a systolic blood pressure of 300 mm. of mercury, after all attempts at relief by medicinal measures had failed. The blood pressure fell in the first three days after operation to 210 and then remained more or less stable around 200, with disappearance of most of the associated symptoms. Another report six months later showed that this improvement had been maintained.

Monier-Vinard and Desmarest [4] in 1930 reported the removal of the right suprarenal from a woman who had suffered for ten years with intolerable hypertensive symptoms, from the time of the menopause. In this case recourse was had successively to spinal anesthesia, suprarenalectomy, radiotherapy and lumbar puncture. The removal of one suprarenal reduced a blood pressure of 320 systolic, 140 diastolic to 220 systolic, 110 diastolic, where it became stabilized for three months, after which it returned to the former figures.

Pieri [5] in 1932, after trying the effects of resection of the right or left splanchnic nerves in five cases of essential hypertension, tried suprarenalectomy in two cases, removing in each case one entire gland. In the case of a man, aged 63, with a systolic pressure of 230 mm. (Pachon), there was a very slight postoperative drop followed by a rapid rise soon afterward, although the clinical symptoms were almost totally relieved, tachycardia on effort and a sense of thoracic pressure disappearing completely. At the end of twenty-two months the blood pressure exceeded 280 mm. (Pachon). In the second case no improvement at all was observed, a blood pressure of 225 (Riva-Rocci) being exactly the same five months later.

On the other hand, the experience of a larger number of writers in connection with the surgical removal of pheochrome tumors of the suprarenal, revealed clinically by attacks of paroxysmal hypertension, throws a different light on the subject. Eisenberg and Wallerstein [6] found fifty-three cases of these tumors in the literature, one half of which were accompanied by hypertension, before the tumors were removed. After removal, the hypertensive attacks and all their associated symptomatology—vomiting, tachycardia, dyspnea, and the like—ceased abruptly.

Cases of this kind have been reported, notably by Oberling and Jung,[7] C. H. Mayo,[8] Pincoffs,[9] Shipley,[10] Wilder,[11] Rabin,[12] and Labbé, Tinel and Doumer.[13] Wilder [11] regards this as without doubt the most important evidence thus far obtained in support of the view that certain forms of hypertension may be due to the secretion of excessive amounts of epinephrine. Rabin [12] found thirty more or less similar cases in the literature, the most suggestive being those in which the hypertension produced by the tumors was paroxysmal.

The completeness with which all symptoms disappeared in these cases when the hyperplastic tissue responsible for hyperfunction of the gland was removed supports my view that the most rational method of treatment of essential hypertension is the surgical excision of sufficient amounts of glandular tissue to relieve the excessive functioning of the gland itself.

PROCEDURE

The operation of partial suprarenalectomy as performed by us consists of removal of about two thirds of each suprarenal and is done in two stages. The por-

1. Crile, G. W.: Recurrent Hyperthyroidism, Neurocirculatory Asthenia and Peptic Ulcer: Treatment by Operations on Suprarenal-Sympathetic System, J. A. M. A. **97**: 1616 (Nov. 28) 1931.
2. Pende, N.: Has Adrenalin Any Physiological Value in the Organism? New York M. J. **118**: 469 (Oct. 17) 1923.
3. Galatà, G.: Di un caso d'ipertensione climaterica colla surrenectomia unilaterale, Riforma med. **45**: 1449 (Oct. 26) 1929; **46**: 588 (April 14) 1930.
4. Monier-Vinard and Desmarest: Hypertension artérielle permanente et primitive avec paroxysmes hypertensifs démesurés: influence de la rachianesthésie, de la surrénalectomie, de la radiothérapie et de la ponction lombaire, Bull. et mém. Soc. méd. d hôp. de Paris **54**: 1084 (June 23) 1930.
5. Pieri, G.: Tentativi di cura chirurgica dell'ipertensione arteriosa essenziale, Riforma med. **48**: 1173 (July 30) 1932.
6. Eisenberg, A. A., and Wallerstein, Harry: Pheochromocytoma of Suprarenal Medulla, Arch. Path. **14**: 818 (Dec.) 1932.
7. Oberling, C., and Jung, G.: Paraganglíome de la surrénale avec hypertension, Bull. et mém. Soc. méd. d. hôp. de Paris **51**: 366 (March 24) 1927.
8. Mayo, C. H.: Paroxysmal Hypertension with Tumor of Retroperitoneal Nerve, J. A. M. A. **89**: 1049 (Sept. 24) 1927.
9. Pincoffs, M. C.: A Case of Paroxysmal Hypertension Associated with Suprarenal Tumor, Tr. A. Am. Physicians **44**: 295, 1929.
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12. Rabin, C. B.: Chromaffin Cell Tumor of the Suprarenal Medulla, Arch. Path. **7**: 228 (Feb.) 1929.
13. Labbé, Tinel and Doumer: Crises solaires et hypertension paroxystique en rapport avec une tumeur surrénale, Bull. et mém. Soc. méd. d. hôp. de Paris **48**: 982 (June 23) 1922.

tion removed includes both medulla and cortex and is taken from the part of the organ remote from the entrance of the blood vessels.

The approach is made from the back through a kidney incision, the kidney being held down with a special retractor. The suprarenal must be recognized and stripped clean of all fat and overlying structures. The portion to be removed is then clamped and excised, the raw surface being covered with a continuous lock-stitch chromic suture.

Spinal anesthesia is employed, and the blood pressure is watched closely throughout the entire operation. If the fall is more than anticipated, ephedrine is promptly given and intravenous saline solution with epinephrine administered in case of collapse. These patients, however, seem to tolerate spinal anesthesia very well, and to date we have not observed any alarming symptoms.

The operation is not severe, and, aside from accidents, we consider it a safe surgical procedure.

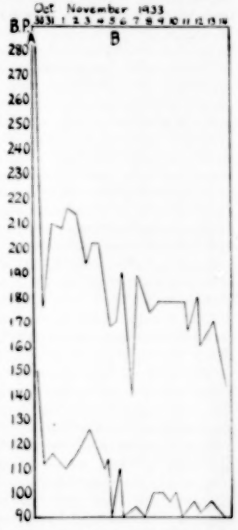

Chart 1.—Drop of blood pressure following bilateral subtotal suprarenalectomy; the spinal anesthesia had entirely worn off before these drops occurred: *A*, right suprarenalectomy, spinal anesthesia; *B*, left suprarenalectomy, spinal anesthesia.

REPORT OF CASES

CASE 1.—Mrs. E. M., a woman, aged 27, married, a nullipara, admitted to the clinic, Oct. 7, 1933, complained of frequent vomiting spells with fulness of the head and dizziness. She said she had been confined to bed for two months previous to observation.

The family history was negative for goiter, carcinoma and tuberculosis; the mother and father were living and well. The patient started to menstruate at 13 years, the periods being irregular, often from six to eight months apart. She had had the ordinary diseases of childhood. There had been no operations.

On examination the patient was well developed and appeared acutely ill, severely nauseated and weak. There were no gross abnormalities of the skin; the mucous membrane was pale and the skin was hot and dry. The pupils were equal, reacting to light and in accommodation. The sclerae and conjunctivae were negative. The ears and nose were normal on external examination. The lips were dry; the tongue was moderately coated. The breath was slightly fetid, its odor suggestive of acetone. The pharynx was red. The upper teeth were artificial, the remaining lower ones in fair condition. The neck was symmetrical. The thyroid was normal to inspection and palpation. Adenopathy could not be found.

The chest was symmetrical. Respiratory excursions were full and equal, negative to percussion and auscultation. The first sound at the apex, bounding and forceful in the fifth interspace, was slightly outside the nipple line. The rate was rapid and the sound not clear but replaced by a slight systolic murmur that was transmitted to the axilla. The second sound at the aortic area was tympanitic in quality. The breasts were normal. The abdomen was symmetrical. No masses or tenderness could be felt. The liver and spleen could not be palpated. No hernia was present. Reflexes were equal and sluggish. There was no edema of the extremities. The blood pressure was 245 systolic, 150 diastolic. Urinalysis in the morning showed: specific gravity, 1.006; albumin negative; sugar, negative. In the afternoon: specific gravity, 1.022; albumin, negative; sugar, negative.

Microscopic examination was negative.

The basal metabolic rate was plus 24. The kidney function showed normal dilution and concentration. The Wassermann reaction of the blood was negative. The red blood cells numbered 4,800,000. The differential count was normal. Urea nitrogen was 15 mg. The blood sugar was 120 mg. two hours after a meal.

We have given a rather comprehensive history to show that we were dealing with so-called essential hypertension. It should also be borne in mind that the patient had been confined to bed at her home 25 miles from Cincinnati for two months previous to the examination.

On admission she was given dextrose to overcome the acidosis. October 17, ten days later, the first operation was performed, which consisted of the removal of three fourths of the left suprarenal under spinal anesthesia.

Before the spinal anesthesia was given the blood pressure was 260 systolic, 150 diastolic.

The systolic blood pressure readings during the operation were: (starting operation) 9:17 a. m., 220; 9:23, 230; 9:30, 180; 9:32, 140; (end) 9:47, 220.

October 18, the day following, the blood pressure was 176 systolic, 130 diastolic; October 19, 174 systolic, 115 diastolic; October 20, 170 systolic, 130 diastolic; October 22, 164 systolic, 114 diastolic.

The second operation was performed, October 23, at which time three fourths of the right suprarenal was removed.

October 25, the blood pressure was 172 systolic, 110 diastolic. October 26, three days after operation, the blood pressure was 165 systolic, 108 diastolic.

It is interesting to note that the patient's diastolic blood pressure did not go below 140 during her long period of bed rest (over two months) previous to operation but dropped to 108 three days after the second operation and has continued to fall to the time of writing.

CASE 2.—Miss A. C., aged 55, single, a nurse, complained of headaches and dizziness. The father had died at 60 of pneumonia; the mother died at 72 of senility.

Five years previous to entrance to the hospital, the patient was refused life insurance because of high blood pressure, although at that time she was feeling well. About one year later she began having severe, persistent headaches with dizziness. Later these attacks were accompanied by hot and cold flashes. Cardiac action became forceful, accompanied with shortness of breath.

The menopause occurred at 52. The blood pressure on the patient's entrance to the hospital was 230 systolic, 140 diastolic. The patient was rather obese. The basal metabolic rate was plus 28.

Urinalysis in the morning showed: specific gravity, 1.008; albumin, negative; sugar, negative. In the afternoon it showed: specific gravity, 1.017; albumin, negative; sugar, negative.

The Wassermann reaction of the blood was negative. Nitrogen was 14.6 mg. Nonprotein nitrogen was 31.26 mg.

Left suprarenalectomy was performed, Nov. 21, 1933; right suprarenalectomy was performed December 1.

A pheochrome cortical tumor about the size of a marble was found in the left suprarenal. Slides of both suprarenals showed lipoidosis of the cortex with medullary hyperplasia.

Immediately following the first suprarenalectomy the diastolic pressure dropped to below 100 mm. of mercury and has remained there to date. At the last reading, December 17, the pressure was 150 systolic, 82 diastolic.

In six cases in which we have operated to date, exploring twelve glands, cortical tumors were present twice.

COMMENT

According to Goldzieher,[14] who has conducted experimental studies on the suprarenals for more than twenty years, the removal of an entire gland, followed later by partial resection of the second gland, does not interfere in the least with the well being of the animal operated on. He found that not more than a fourth of one gland is needed to keep an animal alive indefinitely, and the Cristianis[15] insist that life can be maintained on even less than this.

It has been our own experience that patients tolerate perfectly the removal of from two thirds to three fourths of each gland, a suitable period for recovery being allowed to elapse between the respective procedures on the two individual organs.

The view that hypertension is the result of pathologic changes in the suprarenals was first suggested by Josué[16] and by Vaquez,[17] both of the French school, in 1904. Vaquez dared, on the basis of a case that he had studied anatomically, in which a patient with hypertension was found to have a hyperplastic suprarenal on one side, to formulate the hypothesis that "hypertension is caused by substances capable of provoking excessive vasoconstrictor phenomena, and that these can be discovered only in certain products elaborated by the glands of internal secretion and, in particular, by the suprarenal capsules."

Schur and Wiesel,[18] in 1907, expressed the view that there is a close connection between the problem of epinephrine formation and an associated hypertrophy of the suprarenal gland in all states attended with increased blood pressure, and that this is revealed not only by a chemically demonstrable increased epinephrine content but also morphologically by an increase of chromaffin substance, by the appearance of extensive cell connections in the suprarenal medulla and by multiplication of immature medullary cells.

In 1909, Philpot,[19] after a study of twenty-seven cases of hypertension, reported that the suprarenal medulla was enlarged in nearly every case.

In the last decade, however, the view that pathologic changes of the suprarenals had any connection with hypertension was generally discounted by laboratory workers. Dietrich and Siegmund,[20] after a survey of the literature, considered the existence of a true medullary hypertrophy as still a debated question. Although admitting that there had been isolated cases of this phenomenon, they regarded these as exceptional and concluded that, whereas hyperplasia of the cortex is common enough, the medulla is very little subject to hyperplasia and that no relationship can be discovered between the development of medullary substance and any bodily condition or constitutional disease.

Recently, however, on the basis of new and comprehensive studies, Goldzieher[21] has summarized, as follows, the accumulating evidence pointing to changes in the medulla that serve as the forerunners of hypertension: (1) increased epinephrine content of the glands in states of hypertension, as demonstrated by Ingier and Schmorl[22] and by Goldzieher;[21] (2) hypertrophy of the musculature of the suprarenal veins, demonstrated by Goldzieher and Sherman[23] and by Allen;[24] (3) morphologic changes of the suprarenal cortex,[25] and diffuse hyperplasia of the suprarenal medulla.[26]

Thus, Allen[24] observed in cases of hypertension that there was hypertrophy of the muscles of the suprarenal veins, which he thought in all probability indicated increased functional activity, the result of sympathetic overactivity. He found that the veins of the gland have, in cases of hypertension, a ratio of muscle to lumen twice as great as that in cases of normal blood pressure, which theoretically would indicate (1) increased function of the suprarenal glands, (2) over-

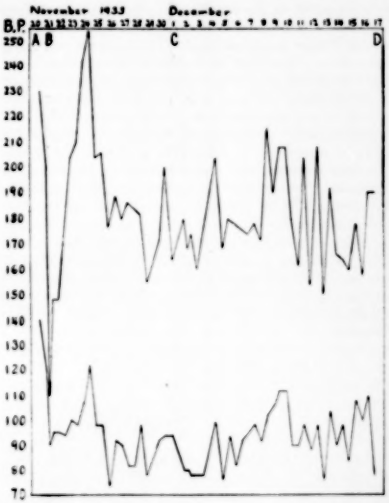

Chart 2 (case 2).—Initial drop, secondary rise and maintenance of low diastolic pressure: *A*, date of admission; *B*, left subtotal suprarenalectomy, spinal anesthesia; *C*, right subtotal suprarenalectomy, spinal anesthesia; *D*, date of dismissal.

activity of the sympathetic nervous system, and (3) the effect of noxious substances in the blood stream. The fact that the total area of the lumens of all the suprarenal veins is greater in cases of hypertension than in those with normal blood pressure shows that there is a higher degree of vascularization in the former, which, according to Allen, probably indicates a higher level of functional activity. In his opinion, these observations are distinct evidence of a close relationship between increased functional activity of the suprarenal glands and a state of hypertension.

14. Goldzieher, M. A.: The Adrenals, New York, Macmillan Company, 1929, p. 30.
15. Cristiani, H., and Christiani, A.: Recherches sur les capsules surrénales, J. physiol. et path. gen. **4**: 838, 1902.
16. Josué, Otto: Capsules surrénales, hypertension, athérome, Bull. et mém. Soc. méd. d. hôp. de Paris **21**: 139, 1904.
17. Vaquez, Henri: Hypertension, Bull. et méd. Soc. méd. d. hôp. de Paris **21**: 120, 1904.
18. Schur and Wiesel: Physiologie und Pathologie des chromaffinen Gewebes, Wien. klin. Med. **20**: 699, 1907.
19. Philpot, A.: An Investigation of the Histological Conditions of the Suprarenal Glands in Conditions Associated with High Blood Pressure, Quart. J. Med. **3**: 34, 1909-1910.
20. Dietrich, A., and Siegmund, H.: Die Nebenniere und das chromaffine System, in Henke, F., and Lubarsch, O.: Handbuch der speziellen pathologischen Anatomie und Histologie, Berlin, Julius Springer **8**: 985.
21. Goldzieher, M. A.: Nodular Hyperplasia of Adrenal Medulla, Endocrinology **16**: 20 (Jan.-Feb.) 1932.
22. Ingier, A., and Schmorl, G.: Ueber den Adrenalingelhalt der Nebennieren, Deutsches Arch. f. klin. Med. **104**: 125, 1911.
23. Goldzieher, M. A., and Sherman, Irving: Hypertrophy of Muscle in Suprarenal Vein in Hypertension, Arch. Path. **5**: 1 (Jan.) 1928.
24. Allen, E. V.: The Suprarenal Glands and Hypertension: A Study of the Veins Within the Suprarenal Glands, Ann. Int. Med. **3**: 153 (Aug.) 1929.
25. Landau, M.: Die Nebennierenrinde, Jena, 1915.
26. Wiesel, J.: Zur Entwicklung der menschlichen Nebenniere, Zentralbl. f. Physiol. **15**: 614, 1902. Goldzieher.[21]

Similar studies conducted by Goldzieher and Sherman [28] showed that both the muscle of the central vein and the single muscle bundles of the small venules participate in the hypertrophy. Injection of the suprarenals through the central veins in patients with hypertension revealed a different distribution of the injected dye from that observed in the controls.

The fact that it was not possible to demonstrate by laboratory methods the presence of epinephrine in the arterial blood has been used as a clinching argument by the opponents of this view of a relationship between medullary pathologic changes and phenomena of hypertension. "No one," admitted Shipley [10] in 1929, "has proven up to the present that an increase of epinephrine is found in the blood in patients with hypertension. Many clinical observations in patients with chromaffin cell tumors indicate that this is true, but the proof has not been forthcoming."

Very recently, however, Kuré [27] and his co-workers have found a new method by which this demonstration has at last been accomplished. By strictly excluding oxygen, which destroys epinephrine, from the blood during the taking of the measurements, they succeeded in demonstrating the presence of the vasoconstrictor substance in the arterial blood. They found that the substance cannot be measured until it is present in amounts in excess of 1:2,500,000 in the whole blood; that oxygen destroys it; that addition of hydrochloric acid increases it, and that it is present in larger amounts in the arterial blood of hypertonic than in that of normal individuals. The substance was always present in the arterial blood in rather high degree, but not in standing blood nor in venous blood. Reasoning that, if hypertension in essential hypertonia is produced by hypersuprarenalinemia, this excess must inevitably be decreased by administration of atropine, which inhibits its liberation into the blood, these workers were able to demonstrate by actual measurements that this decrease occurs after such administration of atropine.

It is therefore finally established in the laboratory that human arterial blood contains epinephrine and that this epinephrine is found in increased quantities in the blood of hypertensive subjects.

Goldzieher [21] has lately drawn attention to the occasional finding of hyperplastic nodules in the pheochrome tissue of the suprarenal. He reports four such cases, in all of which there was either a present state of hypertension or indications of an earlier condition of this kind. The nodules were quite comparable to the nodular growths characteristic of hyperplastic processes in other glandular organs. The appearance of this nodular hyperplasia in addition to diffuse hyperplasia in subjects with hypertension or a history of past hypertension again raises the question whether their occurrence is only incidental here or might be expected with some degree of regularity. Since hyperplasia of other glandular organs has been regarded ordinarily as adequate morphologic evidence of their increased function, it seems unnecessary to look for further proof that the same relations hold true for the suprarenals.

Taking all the evidence into account, we feel, therefore, that the establishment of a clear relationship between essential hypertension and overproduction of epinephrine, comparable to that existing between hyperthyroidism and oversecretion of thyroxine, justifies our contention that the most logical way to reduce essential hypertension is to reduce the amount of superfluous secreting tissue in the suprarenal gland itself.

The case studies of partial suprarenalectomy that we have carried out have been so uniformly satisfactory that we feel that we are now relieving patients who previously were doomed to die, and we are accordingly publishing this report with the hope that the work will be carried on by others in carefully selected cases.

27. Kuré, K.; Nakaya, T., Murakami, S., and Okinaka, S.: Hyperadrenalinamie bei essentieller Hypertonie und ihre Behandlung durch Atropin, Klin. Wchnschr. **12**: 454 (March 25) 1933.

CONCLUSIONS

1. An analogy exists between the overactivity of the suprarenals, due to hypersuprarenalism, and the overactivity of the thyroid, due to hyperthyroidism.

2. Partial suprarenalectomy gives results in hypertension comparable to the results of thyroidectomy in hyperthyroidism.

3. In some of our cases, partial suprarenalectomy relieved all symptoms of hypertension.

4. There is a relation between hypersuprarenalism and hypertension; in states of essential hypertension it is always possible to demonstrate hyperplasia of the suprarenal medulla.

210 West Ninth Street.

NEGATIVE EFFECT OF PROLONGED ADMINISTRATION OF OVARIAN SUBSTANCES IN HEMOPHILIA

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The attempt to treat hemophilia by ovarian extract is not new. As early as 1904, Grant [1] recorded clinical improvement in a patient with hemophilia following the administration of small amounts of an ovarian extract. Wright [2] in 1909, mentioning possible means of combating this inherited defect, skeptically commented on the possibility of administering ovarian extract to male bleeders "with a view of endowing them with the mysterious physiological advantage which, in bleeder families, attach to the female sex." In 1923 Hynek [3] suggested that the production of antithrombin was controlled by the internal secretions of the sex glands. He reported normal clotting of hemophilic blood following injection of corpus luteum. B. and M. Gonzalez-Alvarez [4] in 1925 and Samson-Himmelstjerna [5] in 1926 discussed the theoretical possibilities of treating hemophilia by ovarian extract. Neihans [6] in 1930 treated two hemophilic patients with ovarian implant and observed improvement following the implantation of ovary without corpus luteum, whereas no benefit followed the implantation of whole ovary.

Recent interest in the treatment of hemophilia with estrogenic substance has been stimulated by the reports

From the Thorndike Memorial Laboratory, Second and Fourth Medical Services (Harvard), Boston City Hospital and the Department of Medicine, Harvard University Medical School.

1. Grant, L.: On Hemophilia and Its Treatment, Lancet **2**: 1279 (Nov. 5) 1904.
2. Wright, A. E.: Hemophilia, in Allbutt's System of Medicine, London **5**: 918, 1909.
3. Hynek, K.: Nouvelles considérations sur l'hémophilie, Ann. de méd. **14**: 122 (Aug.) 1923.
4. Gonzalez-Alvarez, B., and Gonzalez-Alvarez, M.: Hemophilia, Siglo méd. **75**: 7 (Jan. 3) 1925.
5. Samson-Himmelstjerna, H. v.: The Nature of Hemophilia and Its Etiological Treatment, M. J. & Rec. **124**: 329 (Sept. 15) 1926.
6. Neihans, Paul: Treatment of Hemophilia, Schweiz. med. Wchnschr. **60**: 18 (Jan. 4) 1930.

of Birch.[7] She has reported nineteen cases of hemophilia in which from 15 to 80 grains (1 to 5 Gm.) daily of ovarian preparations was given subcutaneously, intramuscularly and orally over long periods of time.[7c] In nine of these patients she observed a good response to ovarian therapy, in nine others a definite but less marked improvement and in one no obvious response. In these cases the effect was both general, as shown by an increase in weight, vitality and hemoglobin, and specific, as shown by a decrease in the number and severity of the hemorrhages and a lowered blood coagulation time. Foord and Dysart [8] Kimm and Van Allen,[9] and White [10] have reported immediate cessation of hemorrhage and diminution of coagulation time following the intramuscular injection of ovarian extract or estrogenic substance. Kugelmass [11] has observed that while therapy with the female sex hormone preparation "produces no change in the concentration of the clotting substances from the levels characteristic of hemophilic subjects" and has not diminished the tendency to bruising, it has decreased the tendency to bleeding following natural trauma and has diminished periodic effusions. Key,[12] without presenting specific data, felt that the condition of two cases of hemophilia he studied was not influenced by the administration of ovarian extract. Bernstein [13] reported symptomatic relief in two hemophilic patients after the intramuscular injection of small amounts of whole blood from menstruating women. He states that ovarian extract had been given previously to these patients without change in their joint disorders. Blaylock,[14] in reporting the amputation of an arm of a patient with hemophilia, mentioned the daily subcutaneous administration of an ovarian preparation obtained from the fetal fluid of cattle. One week later, the coagulation time of the blood was slightly longer than before ovarian therapy was instituted.

More recently, Brown and Albright [15] have reported the treatment of a 42-year old hemophilic patient with injections of two preparations of estrogenic substance over a period of three days without significant change in the coagulation time. Estrogenic substance was demonstrated in the urine of this patient before treatment and in greatly increased amounts during the administration of the hormone.

The theory that has prompted these repeated attempts to control hemophilic bleeding and blood-clotting mechanisms by the administration of ovarian extracts and the estrogenic factor is not without a certain speculative attraction. The generally accepted belief, substantiated by studies of cytologists and geneticists, is that the character of inherited traits depends on the character and behavior of the chromosomes. Inherited traits may be sex linked, sex limited or independent of sex. The work of Wilson, Morgan, and other students [16] of the subject has shown that in human beings the male has only one x-chromosome, whereas the female has two. Certain traits including such conditions as hereditary optic atrophy, color blindness and hemophilia are believed to be transmitted in the x-chromosomes. These conditions are called sex-linked defects in distinction to cases of simple heredity, in which the determiners are located in other chromosomes. Certain traits, such as the growth of facial hair, are also independent of the x-chromosomes but are termed sex-limited characteristics, owing to the influence exerted on them by hormones from the sex glands. It is improbable that the administration of potent ovarian substance or of estrogenic substance could exert a fundamental influence on the existence of hemophilia. It is logical to speculate whether or not the bleeding manifestations of the disease might be inhibited temporarily by providing the hemophilic male with substances that can be demonstrated in females and normal males but lacking in males with hemophilia. Such a substance, if effective at all, conceivably might act either on the circulating blood to produce an immediate and transient effect or on the faulty elements of the blood of hemophilic patients at their site of formation, thus to produce a delayed and probably more prolonged effect.

Birch [7b] has reported the production of estrus in rats injected with extracts of the urine of normal men, whereas no estrus was produced in rats injected with extracts of the urines of seven hemophilic males and of two transmitters (females) of hemophilia. From these observations she concluded that the urine of hemophiliacs is lacking in estrogenic substance. To be of undoubted significance these results must be confirmed in every case of proved and active hemophilia so tested. The demonstration of estrogenic principle in an undoubted case of hemophilia would tend to disprove the responsibility of that substance for the immunity to hemophilic manifestations possessed by females. Contrary to Birch's observations, the estrogenic factor has been demonstrated consistently in the urines of five of our patients (no estrogenic factor determinations were carried out in cases 4 and 7) in amounts usually greater than those contained in the urines of normal males.[17] Brown and Albright [15] also found estrogenic substance in the urines of their hemophilic patient before treatment.

The present communication reports the results observed in seven hemophilic patients either fed large quantities of ovarian tissue or given by mouth or parenterally various extracts of ovary and estrogenic substance for from four to eleven weeks.

These patients exhibited classic manifestations of hemophilia dating from infancy or early childhood, and in each instance there were other male members in the family who were affected similarly. Their ages varied from 14 to 36 years. All had suffered repeated hemorrhages into their joints with resulting deformities and limitation of motion of one or more joints. Morphologic examination of the blood in no case revealed significant abnormalities except a slight degree of hypochromic anemia. Blood platelets in each case were normal or increased in number. Three of the seven patients (patients 1, 2 and 5) had been treated in 1931

7. (a) Birch, Carroll L.: Hemophilia, Proc. Soc. Exper. Biol. & Med. **28**: 752 (April) 1931; (b) Hemophilia and the Female Sex Hormone, J. A. M. A. **97**: 244 (July 25) 1931; (c) Hemophilia, ibid. **99**: 1566 (Nov. 5) 1932.

8. Foord, A. G., and Dysart, B. R.: Treatment of Hemophilia by an Ovarian Extract by Birch's Method, J. A. M. A. **98**: 1444 (April 23) 1932.

9. Kimm, H. T., and Van Allen, C. M.: Hemophilia: Prevention and Treatment of Bleeding with Ovarian Extract, J. A. M. A. **99**: 991 (Sept. 17) 1932.

10. White, C. E.: Treatment of Hemophilia with Theelin, J. Oklahoma M. A. **25**: 304 (July) 1932.

11. Kugelmass, I. N.: The Management of Hemorrhagic Problems in Infancy and Childhood, J. A. M. A. **99**: 895 (Sept. 10) 1932.

12. Key, J. A.: Hemophilic Arthritis, Ann. Surg. **95**: 198 (Feb.) 1932.

13. Bernstein, M. A.: The Treatment of Joint Lesions in Hemophilia by Means of Whole Blood from Menstruating Women, J. Bone & Joint Surg. **14**: 659 (July) 1932.

14. Blaylock, Alfred: Amputation of Arm of Patient with Hemophilia, J. A. M. A. **99**: 1777 (Nov. 19) 1932.

15. Brown, R. L., and Albright, Fuller: Estrin Therapy in a Case of Hemophilia, New England J. Med. **209**: 630 (Sept. 28) 1933.

16. Castle, W. E.: Genetics and Eugenics, ed. 4, Cambridge, Mass., Harvard University Press, 1930.

17. The content of estrogenic substance of the urine was determined by Drs. G. V. and O. W. Smith in the Fearing Research Laboratory of the Free Hospital for Women, Brookline, Mass. These results will be reported subsequently.

with large amounts of liver without objective benefit, as reported by Marlow.[18]

METHODS AND MATERIALS USED

In determining the blood coagulation time, both venous blood and capillary blood were used. All determinations were carried out at room temperature. A modification of the method of Lee and White[19] was used for the venous blood. Five cubic centimeters of

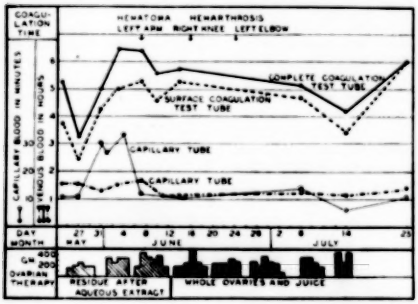

Chart 1.—Observations on the blood coagulation time in case 1 while ovarian therapy was being given.

blood was drawn from an arm vein into a syringe that had been rinsed previously with physiologic solution of sodium chloride, care being taken to cause as little admixture of tissue juice as possible. One cubic centimeter of this blood was dropped into each of five test tubes 8 mm. in diameter, which also had been rinsed with physiologic solution of sodium chloride. The first tube was tilted at intervals of fifteen minutes until it could be inverted without its surface contour being disturbed. This procedure was then carried out on each succeeding tube until all could be inverted without having fluid run at the surface. This end point was recorded as the time of surface coagulation. At this time the blood cells, which had settled to the bottom of the tube, still continued to flow when the tube was tilted. The period of observation was continued until the sediment of cells showed no motion when the tube was tilted. This was recorded as the time of complete coagulation. These two end points are very close together normally and widely separated only when delayed coagulation of the blood is present or when the cells have settled before the first solid clot forms. They can be distinguished readily in normal blood if it is centrifugated rapidly for two or three minutes before clotting occurs.

The coagulation time of venous blood in a capillary tube was determined also. For this determination a tube 10 cm. long and approximately 1 mm. in diameter was nearly filled by capillary attraction with venous blood immediately after withdrawal. At intervals of five minutes the capillary tube was tilted and the movement of the column of blood was observed. When the movement became sluggish, pieces were broken from the end of the capillary tube at intervals. The time at which a fibrin thread could be drawn out of the tube was considered the end point. The coagulation time of capillary blood obtained from puncture of an ear lobe was determined by means of a capillary tube in the same manner as for venous blood.

The coagulation times of the venous and capillary blood from our patients were determined at frequent intervals during the administration of the following preparations of ovarian substance or estrogenic substance, which were given for various periods of time as indicated, and as recorded in the charts:

1. Theelol, orally to patients 1 and 2.
2. Soluble ovarian substance, intramuscularly to patient 4.
3. Ovarian substance-desiccated whole ovary, orally to patient 3.
4. Fresh ground raw whole beef ovary (a small residue of connective tissue was discarded), orally to patients 1 and 4.
5. Aqueous extract from fresh whole beef ovary, orally to patient 2. This extract was prepared by adding from 200 to 400 cc. of water to ground ovaries and shaking in a mechanical shaker for two hours at room temperature. After straining, the juice expressed in the grinding was added to the aqueous extract for administration.
6. The solid residue of ovarian tissue after water extraction, orally to patient 1.
7. Ovarian substance, orally to patients 1, 5 and 6.
8. Theelin, subcutaneously to patients 3 and 7.

RESULTS OF TREATMENT

It is evident from a study of the accompanying charts that no significant changes occurred in the coagulation time of either the venous or the capillary blood of these patients which could be attributed to any one of the various forms of ovarian substance or estrogenic substance administered. Six of the patients received large amounts (quantities are shown in the charts) of one or another form of ovarian substance for from twenty-eight to eighty-one days. Patient 7 received theelin subcutaneously while in a severe bleeding phase, which terminated fatally in three days.

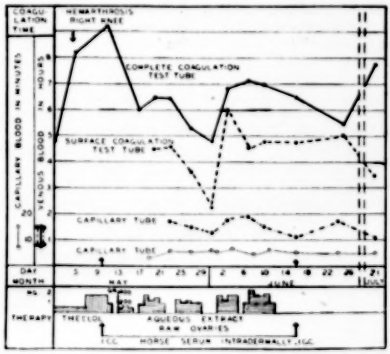

Chart 2.—Observations on the blood coagulation time in case 2.

Patient 1 received 0.4 mg. (200 rat units) of theelol by mouth daily for a period of nine days, and then 0.8 mg. (400 rat units) daily for eighteen days, with no significant reduction in the coagulation time of his venous blood. Chart 1 shows the variations in the coagulation time of his blood immediately following this twenty-seven day period when, over a period of eighteen days, he was given the residue after aqueous extraction of 3,980 Gm. of ovary, a daily average of residue derived from 221 Gm. of whole ovary. This

18. Marlow, A.: The Negative Effect of the Administration of Liver in Hemophilia, Bull. Johns Hopkins Hosp. **49**: 49 (July) 1931.
19. Lee, R. I., and White, P. D.: A Clinical Study of the Coagulation Time of Blood, Am. J. M. Sc. **145**: 495 (April) 1913.

was followed by the administration of a total of 5,989 Gm. of fresh, raw ground, whole ovary over a period of thirty-two days, an average of 187 Gm. a day. These combined periods covered eighty-one days, during which not only did his coagulation time fail to diminish but he suffered one spontaneous hematoma and two hemarthroses.

Patient 2 (chart 2) received a total of 4,800 rat units of theelol by mouth over an eleven day period, after

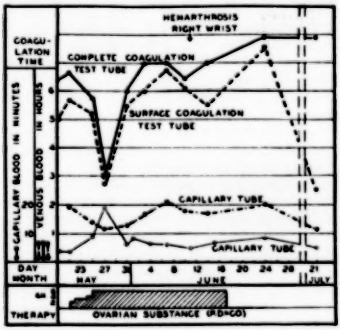

Chart 3.—Observations on the blood coagulation time in case 3.

which he was given the aqueous extract derived from 5,521 Gm. of ovaries over a period of thirty days, a daily average of extract derived from 184 Gm. of whole ovaries. In view of the occurrence of a hemarthrosis, it did not seem justifiable to deter the administration of horse serum to which he had been sensitized previously. As shown by Eley and Clifford [20] and also by Marlow,[18] this procedure has little or no effect on the coagulation time of venous blood but shortens the clotting time of capillary blood, and it was thus not a probable factor in the shorter coagulation time of the venous blood observed after its administration.

Patient 3 (chart 3) was given desiccated ovarian substance orally, 2 Gm. for one day, 3 Gm. on the second and third days, 4 Gm. on the fourth day, and thereafter 6 Gm. daily for twenty-four days. This total amount, given over a period of twenty-eight days, is reported by the manufacturer to be derived from 936 Gm. of whole ovary, making a daily average derived from 33.4 Gm. of the gland. Six months after the period shown in chart 3, the patient was given 1 cc. (50 rat units) of theelin subcutaneously daily for seven days. During the latter period the coagulation time of the venous blood dropped from ten hours to seven hours and thirty-four minutes. One week after the treatment was discontinued, the coagulation time was six hours. Although this is a 40 per cent decrease in the coagulation time, it is no greater a drop than is seen frequently without therapy and does not seem attributable to therapy with estrogenic principle in view of the continued drop after theelin was omitted.

Patient 4 (chart 4), after the daily intramuscular injection of 1 cc. of soluble extract of ovarian substance for eighteen days and 2 cc. daily for the subsequent four days, received orally 6,189 Gm. of whole raw ground ovary over a thirty-two day period, a daily average of 193 Gm. The coagulation time was unchanged.

Chart 5 shows the complete coagulation times of the venous blood observed in cases 1, 5 and 6 during the administration of ovarian substance by mouth over periods of forty-four, seventy, and forty-one days, respectively. The usual daily dose of 8 Gm. of this substance is reported by the manufacturer to be the approximate equivalent of 48 Gm. of the fresh glandular substance. These periods of observation started eleven weeks after patient 1 had received the treatment shown in chart 1, and ten weeks after patient 5 had received anterior pituitary-like principle from the urine of pregnancy for seven days. Patient 6 had received no ovarian therapy previously.

In case 6, the coagulation times of one hour and on the following day of four hours, observed eighteen weeks after therapy was stopped, were shorter than any observed during or immediately following treatment. Coagulation times of five hours and four hours and thirty-six minutes were observed six months after treatment. Six days after the last observation of the coagulation time in case 1 recorded in chart 5, it rose to seven hours and forty-five minutes to fall a week later to three hours and fifty-five minutes, a level identical with that observed on the thirty-fifth day of treatment.

During these periods of observation all three patients were excreting estrogenic substance in amounts varying from less than 2 rat units to 12 rat units per forty-eight hour quantity of urine. In no case was there any demonstrable correlation between the amount of estrogenic substance excreted and the coagulation time of the blood.

An additional patient (patient 7) who was bleeding severely was given a total of 5 cc. (250 rat units) of theelin in three intramuscular injections over a three-day period. This resulted in no apparent effect on his bleeding. In spite of repeated blood transfusions and injections and local applications of a thromboplastic substance and hemostatic serum, he continued to bleed and died from hemorrhage.[21]

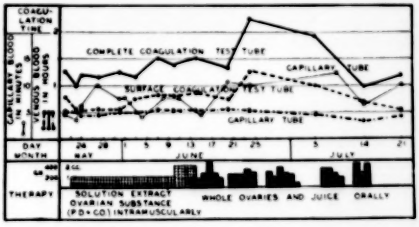

Chart 4.—Observations on the blood coagulation time in case 4.

COMMENT

The amount of ovarian substance given in six of these cases of hemophilia was greater than any recorded in the literature given in similar cases. The periods of observation would seem long enough to demonstrate any change in coagulation time that such therapy might effect. The fluctuations of blood coagulation time observed are of a magnitude encountered frequently in hemophilic patients under no specific form

20. Eley, R. C., and Clifford, S. H.: Hemophilia: Treatment by Protein Sensitization, Am. J. Dis. Child. 42:1331 (Dec.) 1931.

21. Acknowledgment for permission to include this case is gratefully made to the Third Medical Service (Tufts) of the Boston City Hospital.

of therapy, as was demonstrated in these cases during control periods. Case 1 has been observed for twenty-four years; cases 4 and 5 have been observed for six years. During these years when various forms of treatment were given or when no particular treatment was given, the fluctuations of the blood coagulation time have been fully as great as has been recorded during the present series of observations. In no case in which ovarian therapy was given did the coagulation time of the venous blood approximate a normal figure.

In two instances (cases 3 and 7) the subcutaneous injection of estrogenic substance (theelin) for from three to seven days failed to produce any immediate effect on the coagulation time in either case or on the severe bleeding in case 7.

Three of our patients felt that they were subjectively improved by treatment. Patient 5 gained 29 pounds (13.2 Kg.) while in the hospital. However, none of our patients showed objective evidence of improvement other than could be expected to result from rest, an adequate diet, physical therapy and general measures of hygiene. In four of the patients (1, 3, 4 and 5) hemarthroses developed late in the course of ovarian treatment and in only one instance (case 5, chart 5) was there any demonstrable infection that might be

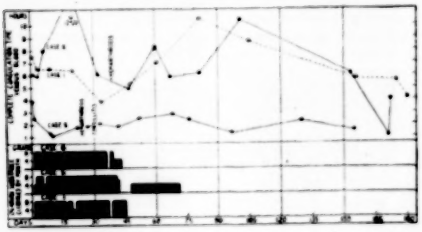

Chart 5.—Observations on the complete coagulation time of the venous blood in cases 1, 5 and 6 during and after the oral administration of ovarian substance.

considered a precipitating factor. In no instance could we obtain a history of unusual trauma, which might have caused these hemarthroses.

SUMMARY

The coagulation time of the blood of seven patients with hemophilia was observed repeatedly during treatment with ovarian substance or estrogenic substance. Large amounts of one or another of eight different preparations were given over periods of from twenty-eight to eighty-one days. In no instance was the coagulation time of the venous blood found to be depressed as the result of such therapy. Theelin (estrogenic substance) administered subcutaneously to two patients for from three to seven days neither stopped bleeding nor reduced the clotting time.

Estrogenic substance was demonstrated consistently in the urines of our patients both under ovarian therapy and during control periods. No correlation could be established between the quantity of estrogenic substance excreted in the urine and the fluctuations of the blood coagulation time.

No clinical improvement was noted which could be attributed to ovarian therapy. In four of the patients hemarthroses developed without obvious trauma or infection late in the course of treatment.

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BLOOD GROUPS AND THERAPEUTIC MALARIA

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Since malarial therapy for syphilis of the central nervous system has come into vogue, several problems of practical importance have arisen which have interested the physician employing this mode of therapy. For therapeutic as well as for economic reasons, it is highly desirable that the course of malarial treatment be as short as possible. Usually such a course, if successfully carried out, consumes from eight to ten days, with an incubation period of four days or less. Wide variations in the incubation period, however, have often prolonged the course of treatment, making it unsatisfactory from an economic point of view. In fact, frequently the patient has to be kept in the hospital for weeks because the malarial fever cannot be induced in spite of repeated injections of blood containing virulent parasites. This has been ascribed to the following causes: individual factors;[1] the manner of inoculation, i. e., subcutaneously or intravenously;[1a] the stage of development of the parasite in the donor's blood;[2] the amount of blood injected;[3] the strain of the organism; the temperature of the environment,[4] and the compatibility between the donor's red blood cells and the recipient's serum. In 1927, Wendlberger,[5] from a study of the blood groups of donors and recipients in fifty cases in which malarial therapy was used, found that in some instances in which the donor's cells were incompatible with the recipient's serum malarial fever could not be induced at all, while in others it was induced only after a prolonged incubation time. The success or failure in the attempt to induce malaria in these cases was found to depend on the agglutinin titer of the recipient's serum.[6] Following Wendlberger's work, a number of similar investigations were carried out by Wethmar,[7] Pilcz,[8] Arzt and Fuhs,[9] Herrmann and Hlisnikowski[10] and Walter.[11] With the exception of Walter's studies, the observations of Wendlberger have been almost unanimously confirmed.

An interesting phenomenon that has come to light in the therapeutic application of induced malaria, which

From the Departments of Pathology, Jewish Hospital of Brooklyn (Dr. Max Lederer, director), and the Brooklyn State Hospital.

1. (a) Gertsmann, Josef: Die Malariabehandlung der progressiven Paralyse, Vienna, Julius Springer, 1925. (b) Kihn, Berthold: Die Behandlung der quartären Syphilis mit akuten Infektionen, Munich, J. F. Bergmann, 1927. (c) O'Leary, P. A., and Welsh, A. L.: The Treatment of Neurosyphilis with Malaria, J. A. M. A. **101**: 498 (Aug. 17) 1933.

2. von Wagner-Jauregg, Julius: Einige Bemerkungen über Impf-Malaria, Wien. klin. Wchnschr. **40**: 26 (Jan. 6) 1121 (Sept. 8) 1927. Hopf, G.: Die Bedeutung von Blutgruppenkonstellation und Entwicklungsstadium der Plasmodien für Malariatyp und Inkubationszeit, München. med. Wchnschr. **75**: 1755 (Oct. 12) 1928. Horn, L.: Studie über die Malariaparasiten im verträglichen und unverträglichen Serum, Wien. klin. Wchnschr. **42**: 995 (July 25) 1929. Knights, E. M.: The Influence of Blood Groups in Malarial Transfusions, J. Lab. & Clin. Med. **15**: 980 (July) 1930.

3. Doerr, R., and Kirschner, L.: Zur Malariabehandlung der progressiven Paralyse, Ztschr. f. Hyg. u. Infektionskr. **92**: 279, 1921.

4. Hecht-Elada, M.: Zur Impfmalaria der Syphilis, Arch. f. Dermat. u. Syph. **150**: 277, 1928.

5. Wendlberger, J.: Blutgruppen und Impfmalaria, Wien. klin. Wchnschr. **40**: 345 (March 17) 1927; **43**: 932 (July 24) 1930.

6. Obermayer, M., and Wendlberger, J.: Blutgruppen und Impfmalaria, Wien. klin. Wchnschr. **41**: 1304 (Sept. 13) 1928.

7. Wethmar, R.: Blutgruppen und Impfmalaria, Klin. Wchnschr. **6**: 1947 (Oct. 8) 1927.

8. Pilcz, A.: Zur Frage der Blutgruppen und Impfmalaria, Wien. klin. Wchnschr. **40**: 653 (May 19) 1927.

9. Arzt, L., and Fuhs, H.: Zur Malariabehandlung der Syphilis, Arch. f. Dermat. u. Syph. **153**: 464, 1927.

10. Herrmann, G., and Hlisnikowski, H.: Blutgruppen und Verlauf der Impfmalaria, Med. Klin. **24**: 1700 (Nov. 2) 1928.

11. Walter, F.: Ueber den Einfluss der Neosalvarsaninfektionen auf die Inkubationsdauer der Impfmalaria bei Frühsyphilitikern, Dermat. Wchnschr. **88**: 19 (Jan. 5) 1929.

was first described by Korteweg[12] and later by Wethmar, is that of so-called primary fever. This is a remittent fever without chills, appearing about the fourth day after inoculation of the malarial blood and lasting until one or two days before or merging with the actual malarial chills. Although previously unrecognized as such, primary fever is now believed by some to occur in naturally acquired as well as in artificially induced malaria.[13] Wethmar[14] has shown that in induced malaria the occurrence and course of the fever are greatly influenced by the blood group of the donor and of the recipient. Thus he found that when the incubation time was short, primary fever occurred in 100 per cent of the cases and lasted on an average of 3.7 days, while in the cases in which the incubation time was prolonged, only 42 per cent presented primary fever, with an average duration of only slightly more than one day. Since the incubation time is influenced by the compatibility between the donor's cells and the recipient's serum, it follows that the blood groups indirectly affect the frequency of occurrence and duration of the primary fever as well.

The importance of this phenomenon resides in the fact that patients who are too weak to be subjected to a high primary fever may be spared this additional strain by receiving incompatible malarial blood, which would greatly lessen the intensity as well as the possibility of the occurrence of primary fever.

Still another practical problem that has arisen as a result of the widespread use of malarial therapy is the possible danger of emboli, which might result from the injection of incompatible blood. It is conceivable, in fact probable, that incompatible donor's cells, small though the quantity may be, might be agglutinated by the recipient's serum and result in emboli, which may produce infarcts in the lungs. In the presence of a patent foramen ovale this may even result in cerebral embolism. Wendlberger, Wethmar and others have recognized a definite reaction that follows the injection of incompatible malarial blood. This appears soon after the injection and consists of a rise in temperature with chills, nausea and dyspnea. It is significant that these reactions have been observed mainly in cases in which the incompatible blood was injected intravenously.

The American literature, with the exception of a study of twelve cases reported by Knights in 1930, has no information on any of these problems. However, since these problems appeared to be of sufficient importance to warrant further investigation, the present study was undertaken.

One hundred and twenty-seven cases of dementia paralytica were observed. Each patient received 5 cc. of malarial blood intravenously a few minutes after the blood was withdrawn from the donor. The blood groups of donor and recipient were determined according to the method described by Landsteiner.[15] From the time the patient received the blood, the clinical course was carefully observed with regard to the following: (A) incubation period, (B) immediate or delayed incompatibility reactions (rise in temperature, embolic phenomena, dyspnea, gastric distress, chill, suppression of urine, hematuria and the like) and (C) occurrence and duration of primary fever.

A. *Incubation Period.*—The data can be studied best from the accompanying table and chart. In the table the cases have been classified into two groups; namely, those receiving compatible and those receiving incompatible blood, with a record of the incubation period in each. It will be observed that in the former group[16] the average incubation period is 4.30 days, while in the latter it is 8.18 days. That the difference between the average incubation periods of the two groups is not merely apparent but actually significant has been proved mathematically by Dr. A. S. Wiener.[17] The accompanying chart is plotted from the figures in the table and shows more vividly the influence of blood compatibility on the incubation period.

A study of the table further discloses that in addition to the difference in the incubation periods noted in the two groups there is also a wide variation of the incubation period within each group, as evidenced by the large standard deviation. (The standard deviation was calculated to be 3.04 ± 0.24 days in the series receiving compatible blood and 4.76 ± 0.51 days in the series receiving incompatible blood. This variation may be attributed to other factors already enumerated which influence the incubation period. One of the most important of these is individual resistance to malarial infection. Thus O'Leary and Welsh,[16c] in a recent report on a study of malarial therapy in 984 cases of neurosyphilis, found it impossible to induce chills and fever in 10 per cent of the patients inoculated, because of their immunity to malaria. In our series there were

Incubation Period of Injection Malaria in Patients Receiving Compatible and Incompatible Blood

Incubation Period, Days	Patients Receiving Compatible Blood		Patients Receiving Incompatible Blood	
	No. of Cases	Per Cent of Cases	No. of Cases	Per Cent of Cases
1	8	9.8	2	4.4
2	7	8.5	0	0
3	22	26.8	2	4.4
4	15	18.3	3	6.7
5	13	15.9	4	8.9
6	5	6.1	5	11.1
7	4	4.9	7	15.5
8	0	0	5	11.1
9	1	1.2	3	6.7
10	0	0	2	4.4
11	0	0	1	2.2
12	1	1.2	2	4.4
13	1	1.2	2	4.4
14	0	0	1	2.2
15	1	1.2	0	0
16	0	0	0	0
17	0	0	1	2.2
18–19	0	0	0	0
20	1	1.2	0	0
21–22	0	0	0	0
23	0	0	2	4.4
Total	79	100	42	100

12. Korteweg, P. C.: First Onset of Malaria, Nederl. Tijdschr. v. Geneesk. **1**: 1622 (April 12) 1924.

13. Manson, Patrick: Experimental Proof of the Mosquito-Malaria Theory, Lancet **2**: 923, 1900. James, S. P.: Rapport sur les premiers resultats fournés par les travaux de laboratoire sur la paludisme en Angleterre, Soc. des Nations, Geneva, 1926.

14. Wethmar, R.: Ueber Anfangsfieber und Inkubation bei der Impfmalaria und der spontanen Malaria, Deutsche med. Wchnschr. **54**: 826 (May 18) 1928.

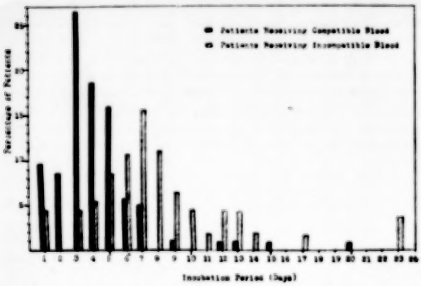
15. Landsteiner, Karl: The Newer Knowledge of Bacteriology and Immunology, Chicago, Jordan & Falk, 1928.

16. This group could be subdivided into two groups; namely, those receiving homologous blood ($O \rightarrow O$, $A \rightarrow A$, $B \rightarrow B$, and $AB \rightarrow AB$), and those receiving heterologous blood (such as $O \rightarrow A$, $O \rightarrow B$, $O \rightarrow AB$, $A \rightarrow AB$, $B \rightarrow AB$). In the former subgroup (forty-six cases), the mean incubation period was 4.64 days, and in the latter (thirty-three cases), 3.85 days, so that there was no significant difference between the two types of cases. This is rather to be expected since it is the donor's erythrocytes and not the serum which contain the malarial parasite.

17. That the difference between the means of the two groups is significant may be proved by calculating the probable error of this difference. The probable error of a mean is given by the formula $P.E._{Mean} = \frac{0.6745\sigma}{\sqrt{N}}$ in which σ represents the standard deviation of the data and N the number of individuals examined. In the group receiving compatible blood, the probable error is 0.22 day, and in the group receiving incompatible blood, 0.48 day. The probable error of the difference between the means is equal to $\sqrt{0.22^2 + 0.48^2} = 0.52$ day. Therefore, the difference between the two means is more than seven times as great as its probable error. Since a difference of such a magnitude could occur by chance only in more than 1,000,000 trials, it is unquestionably significant.

six cases (three in each group) in which malaria could not be induced, in spite of repeated inoculations with malarial blood. These failures were also probably due to the individual resistance to the parasite. It may be added that these cases were not included in the calculations in order to avoid masking the effect of the use of compatible and incompatible bloods.

B. *"Incompatibility" Reactions.*—Untoward reactions consisting of the symptoms already described occurred in eleven cases following inoculation of the malarial blood. In no instance, however, could it be determined with any degree of certainty that these reactions were due to incompatibility between the donor's and the recipient's blood. The donor's and the recipient's blood were compatible in the five instances in which chills and rise in temperature followed within one or two hours after inoculation. One of the severest of these reactions occurred in a case in which both donor and recipient belonged to group A (the subgroup was not determined). In seven cases, hemoglobinuria or hematuria followed the inoculation, but in four of these instances the bloods of donor and of recipient were compatible. Hence the observations of Wendlberger, Wethmar and others regarding blood incompatibility reactions were not confirmed in this study. It is possible that the various other factors that are known to produce untoward symptoms following intravenous injection of blood might have caused the reactions noted by the previous authors as well as by us. Among these causes may be mentioned foreign proteins (in the malarial cells as well as in the blood of the donor), incipient coagulative changes, and chemical contamination of the donor's blood.[18]



Influence of blood compatibility on incubation period of infection malaria.

C. *Primary Fever.*—We have found it quite difficult to determine with certainty the occurrence of primary fever. The temperature curves after inoculation (during the period of incubation) in most cases failed to correspond with those described by Wethmar and the others who have described the phenomenon. In the group of forty-two patients receiving incompatible blood, primary fever developed in only five (or about 12 per cent), while in the group of seventy-nine patients receiving compatible blood, it developed in twelve (15 per cent). These figures are strikingly smaller than those given by Wethmar. The difference may be due to our failure to recognize the phenomenon. In our cases it was found that the temperature curve during the incubation period was frequently too irregular to conform rigidly to the definition of primary fever as stated by its authors.

18. Polayes, S. H., and Lederer, Max: Reactions to Blood Transfusions, J. Lab. & Clin. Med. **17**: 1029 (July) 1932.

SUMMARY AND CONCLUSIONS

A series of 127 cases of dementia paralytica treated with malarial blood was studied in order to determine (*a*) the effect of the injection of compatible or incompatible blood on the incubation period, (*b*) the occurrence of immediate or delayed reactions to incompatible malarial blood, and (*c*) the frequency of occurrence of so-called primary fever. The following conclusions may be drawn:

1. The average incubation period is 4.30 days when the malarial blood injected is compatible and 8.18 days when it is incompatible with the recipient's serum. That this difference is significant was proved by statistical analysis.

Wide variations of the incubation periods were noted in the group of patients receiving compatible as well as in those receiving incompatible blood. These differences may be ascribed to factors other than compatibility or incompatibility of blood.

2. With regard to untoward postinoculation reactions, it was not possible to determine with any degree of certainty that they were due to incompatibility between the donor's and the recipient's blood. Other possible factors may be responsible for these reactions.

3. Primary fever occurred in only 15 per cent of the patients receiving compatible malarial blood. These figures are much smaller than those found by previous investigators. The difference is perhaps due to the fact that it is difficult to recognize this phenomenon because the postinoculation temperature curve is frequently too irregular to conform rigidly to the definition of primary fever.

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NECESSITY FOR REVISING THE COMMON CONCEPTION OF FOCAL INFECTION

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A focus of infecion has been defined as a circumscribed area of tissue infected with pathogenic organisms.[1] General recognition that it can cause systemic or general disease makes its elimination an important part of the treatment of such disease.

COMMON MISCONCEPTION OF FOCAL INFECTION

In the common conception of focal infection, attention seems to be concentrated on the infected tissue rather than on the infecting bacteria. When a physician speaks of eliminating the focus of infection, what he really means is the removal of infected tissue, such as tonsils and teeth, or the opening and draining, or the cleaning out, of an infected cavity, such as a nasal accessory sinus. He apparently fails to realize that, in the upper air passages, at least, infecting bacteria seldom are confined to a circumscribed area of diseased tissue but are present also on adjacent tissues. The germs infecting the tonsil, for instance, may be found on the adjacent mucous membrane of the throat and

Read before the College of Physicians of Philadelphia, Nov. 2, 1933.

1. Billings, Frank: Focal Infection, New York, D. Appleton & Co., 1916, p. 2.

nasopharynx and in the infratonsillar lymphoid tissue. Similarly the micro-organisms infecting a sinus find their way to the nasal and nasopharyngeal mucous membrane. These microbes are not removed by tonsillectomy and sinus treatment or operation but continue to live and multiply, elaborating toxins and infecting distant tissues.

FOCUS OF INFECTION IN TONSILS NOT ERADICATED BY TONSILLECTOMY

Why should so many physicians, including otolaryngologists, state that the focus of infection has been eradicated after tonsillectomy? It is known that the surgeon frequently fails to remove all the tonsillar tissue, leaving behind tonsillar stumps,[2] which constitute as great a focus of infection as did the whole tonsil. Indeed, Rhoads and Dick [2] believe that in many instances the condition resulting from incomplete tonsillectomy is worse than that existing before the operation. Even when a perfect tonsillectomy has been performed it often is followed by a recurrence of tonsillar tissue which may be just as serious a focus of infection as the original tonsil.[3] The lymphoid masses, commonly spoken of as recurrent tonsils [4] but really nothing more than infratonsillar lymphoid tissue that has worked its way upward into the empty tonsillar fossa,[5] are regarded by French [4] as quite as potent a factor of systemic infection as infected faucial tonsils, the same micro-organisms being recovered from the two. Normal appearing tonsillar fossae also may harbor infecting organisms, as I have repeatedly demonstrated,[6] and thus act as foci of infection. I made seventy-four pathogen-selective cultures of apparently clear tonsillar fossae and found infecting bacteria in seventy-three (97 per cent).

FOCAL INFECTION IN THE NASOPHARYNX NOT REMOVED BY OPERATION

When adenoid vegetations in the nasopharynx constitute the focus of infection, adenoidectomy is supposed to eradicate it. Yet tags and remnants after adenoidectomy by skilled physicians were found by Hill [7] in 25 per cent of 409 students over 16 years of age and in 50 per cent of 186 younger children.

The apparently normal nasopharynx frequently becomes the habitat of infecting germs and thus serves as a focus of infection, as I pointed out some years ago.[8] I made 147 pathogen-selective cultures of the nasopharynx in suspected infections of the upper respiratory tract and found infecting organisms in 140 (95 per cent).

Frequently the same infecting bacteria that are present in diseased tonsils are living also in the nasopharynx. I made seventy-eight simultaneous pathogen-selective cultures of diseased tonsils and the nasopharynx, finding the same infecting organism in both cultures in forty-two (54 per cent). The nasopharynx, on the other hand, may contain infecting bacteria that are not present in the tonsils. In eighteen of the seventy-eight cultures (23 per cent) none of the infecting organisms present in the nasopharynx were found in the tonsils. Similarly the tonsils may contain infecting germs that are absent from the nasopharynx. In eighteen (23 per cent) of the cultures the tonsils contained infecting organism not present in the nasopharynx. The nasopharynx may also contain the same infecting organisms that are present in the tonsillar fossae, as occurred in thirty-eight (47 per cent) of eighty-one pathogen-selective cultures which I made simultaneously of each of these areas. In twenty-one (26 per cent) of these cultures no infecting microbe present in the tonsillar fossae was found in the rhinopharynx, while in twenty-two (27 per cent) no infecting organism present in the nasopharynx was found in the tonsillar spaces. It has been my practice in recent years, when searching for foci of infection, to make pathogen-selective cultures in the same tube of the tonsillar spaces and nasopharynx. I made 305 such cultures, in 283 (93 per cent) of which infecting organisms grew up.

FOCI OF INFECTION IN NASAL ACCESSORY SINUSES NOT ELIMINATED BY TREATMENT OR OPERATION

A similar situation exists in regard to infection in the nasal accessory sinuses. When the rhinologist has opened and drained a sinus or has done a conservative or radical operation on it, he believes and reports that he has eradicated the focus of infection. The infecting organisms, however, frequently still remain in or about the treated sinus. I made 230 pathogen-selective cultures of the nares and thirty-five such cultures of the sinuses of patients who had received expert treatment for sinusitis and found infecting organisms in 180 (78 per cent) of the nasal cultures and in twenty (57 per cent) of the sinus cultures. Seventy-five simultaneous pathogen-selective cultures of the nares and the nasopharynx showed the same infecting germ in thirty (40 per cent). In twenty-one (28 per cent) none of the infecting germs present in the nares were found in the nasopharynx and in twenty-four (32 per cent) no infecting organism present in the nasopharynx was found in the nares. Nine simultaneous pathogen-selective cultures were made of the sinuses and the nasopharynx, in one third of which the same infecting organisms were found in the two areas; in another third the infecting organisms in the sinuses were absent from the nasopharynx, and in one third none of the infecting germs in the nasopharynx were found in the sinuses.

But not only is the rhinologist unable to eliminate a bacterial focus of infection in the sinuses; frequently,

2. Clark, J. P.: Results in a Series of Cases of Tonsillectomy at the Massachusetts General Hospital Three to Four Years After Operation, Tr. Am. Laryngol. A., 1913, pp. 43-52. Rhoads, P. S., and Dick, G. F.: Efficacy of Tonsillectomy for the Removal of Focal Infection, J. A. M. A. **91**: 1149-1154 (Oct. 20) 1928.

3. Leskin, Norman, and Pearlman, S. J.: Are Tonsillar Recurrences Entirely Due to Faulty Operative Technic? Arch. Otolaryng. **13**: 37-46 (Jan.) 1931.

4. French, T. R.: Tonsillectomy and Its Recent Revelations: The Nose, Throat, Ear and Their Diseases (edited by Chevalier Jackson and George Morrison Coates), Philadelphia, W. B. Saunders Company, 1929, p. 250.

5. Leskin and Pearlman,[3] French,[4] Grichter, B. B., and Pearlman, S. J.: Lymphoid Tissue in the Tonsillar Fossae Following Tonsillectomy, Ann. Otol., Rhinol. & Laryng. **32**: 860-863 (Sept.) 1923. Speke, L. B.: The Recurring Tonsil, J. Kansas M. Soc. **22**: 321-323 (Nov.) 1922. Baum, H. L.: Complications and Sequelae of Tonsil and Adenoid Operations: Their Prevention and Management, Ann. Otol., Rhin. & Laryng. **29**: 37-49 (March) 1919. McMurray, J. B.: A Study of the Superficial and Deep Lymphoid Tissues of the Hypopharynx, Atlantic M. J. **30**: 63-66 (Nov.) 1926. Long, C. H.: Recurrence of Tonsils After Tonsillectomy, Illinois M. J. **45**: 266-268 (April) 1924. Roberts, E. R.: The Tonsil Problem: Working Hypothesis for General Guidance, Arch. Otolaryng. **6**: 563-568 (Dec.) 1927. Pierce, N. H.: Discussion on the Tonsil Question to Date, Tr. Am. Laryng., Rhin. & Otol. Soc., 1921, p. 267.

6. Solis-Cohen, Myer, and Heist, G. D.: A Method of Distinguishing from Among Various Micro-Organisms Present in a Patient, Those that Are and Those that Are Not Acted upon by That Patient's Whole Coagulable Blood, Pennsylvania M. J. **25**: 27-34 (Oct.) 1921. Solis-Cohen, Myer: Visceral Disease Due to Bacterial Infection of an Apparently Normal Upper Respiratory Tract, J. A. M. A. **83**: 824-829 (Sept. 13) 1924. Boerner, Fred, and Solis-Cohen, Myer: A Study of Pathogen Selective Cultures in Relation to Vaccine Therapy, Am. J. Clin. Path. **2**: 125-131 (March) 1933.

7. Hill, F. T.: Observations Following Adenoidectomy, Arch. Otol. **14**: 775-779 (Dec.) 1931.

8. Solis-Cohen, Myer: The Rhinopharynx as a Site of Focal Infection, Ann. Otol., Rhin. & Laryng. **33**: 935-950 (Sept.) 1924.

according to Skillern,[9] Proetz,[10] Carter [11] and Pond,[12] he fails to cure the sinusitis.

FOCAL INFECTION IN THE ORAL CAVITY NOT ALWAYS REMOVED BY THE EXODONTIST

Focal infection in the oral cavity as a rule can be eradicated by surgery, but it is not always removed when infected teeth are extracted. According to Post,[13] a residual pathologic condition is a most important and often overlooked source of focal infection.

SHOULD THE EXPRESSION "ELIMINATION OF THE FOCUS OF INFECTION" BE APPLIED TO MERE REMOVAL OF INFECTED TISSUE?

In the interest of accuracy should not such expressions as "removal" or "elimination" or "eradication" of the focus of infection be avoided when tonsillectomy or sinus treatment or operation is being described? The physician then would not be influenced by this incorrect and misleading information to abandon his investigation of the upper air passages and in his search elsewhere for the elusive focus even to order sometimes the unnecessary extraction of healthy and useful teeth on the chance that the focus of infection might be there. Realization that the focus of infection had not really been eliminated might minimize his disappointment when no improvement in the systemic disease follows the operative procedure. A result helpful to science would be a lessening of the skepticism as to the etiologic importance of focal infection and of the tendency to assign a greater rôle to factors that may be unimportant or only of secondary significance.

A REVISED CONCEPTION OF FOCAL INFECTION

If the conception of focal infection stressed the bacterial element and regarded the causal germ as the chief infecting agent, the problems involved in its eradication would be better appreciated. It then would not be so difficult, in the absence of recognizably diseased tissue, to conceive of a bacterial focus of infection, produced solely by infecting organisms living on an apparently normal mucous membrane where they multiply and elaborate their toxins. One would realize that surgery alone cannot possibly remove all the infecting organisms, which can be overcome only by the patient's defensive forces.

MEASURES REQUIRED FOR ELIMINATING FOCAL INFECTION

The elimination of a focus of infection requires the production of bactericidins and other antibodies to destroy the infecting bacteria and render their toxins harmless. In most cases it will be necessary at one or more foci to extirpate accessible and removable diseased tissue that has become a favorable soil for the growth of the infecting germs. Sometimes following such removal a patient regains his lost or lowered resistance and recovers from the systemic disease without further medical assistance. Such a striking cure following operation strongly impresses the physician, despite bitter disappointments in other cases, and doubtless has helped to preserve the oft wavering belief in the focal origin of disease. It probably is one reason for the impression that the surgeon can remove a focus of infection. In my experience, however, such favorable results are not the rule.

In most cases the physician must come to nature's aid. Billings [14] recognized this when he recommended not only removal of all primary and, if necessary, all secondary foci of infection but also the building up of the natural defenses of the body.

Before making a diagnosis of focal infection, however, one of course must be certain that the condition is not one of allergy, lack of proper vitamins or endocrine dysfunction.

Among the patients whose condition has been unaffected by operative procedures, a number will improve when their resistance has been raised by hygienic measures. Others will require, in addition, artificial stimulation of specific antibody production by means of vaccine, which must contain the proper specific antigens obtained from the infecting bacteria.

DETERMINING THE INFECTING BACTERIA

The chief objection to vaccine therapy in systemic disease is the difficulty or even impossibility of determining what germ is the cause of the disease and which, if any, of the bacteria at a supposed primary focus is the etiologic factor.

Action of Patient's Fresh, Whole, Coagulable Blood on the Organism Predominating in the Culture in Rosenow's Brain Broth

Organism	Predominating in Brain Broth, Number	Growing in Patient's Blood		Failing to Grow in Patient's Blood	
		Number	Per Cent	Number	Per Cent
Bacillus proteus	2	2	100	0	0
Diphtheroids	1	1	100	0	0
Streptococcus haemolyticus	17	16	94	1	6
Streptococcus viridans	33	26	79	7	21
Staphylococcus (unclassified)	4	3	75	1	25
Staphylococcus aureus	81	57	70	24	30
Friedländer's bacillus	3	2	67	1	33
Streptococcus nonhaemolyticus	75	49	65	26	35
Pneumococcus	2	1	50	1	50
Staphylococcus albus	151	54	36	97	64
Staphylococcus pharyngis	3	1	33	2	67
Streptococcus (unclassified)	3	1	33	2	67
Micrococcus pharyngis sicus	4	1	25	3	75
Bacillus coli	5	1	20	4	80
Total	384	215	56	169	44

In a subacute or chronic infection the mere presence of microbes on or in infected tissue or in the secretion or excretion from it is no indication of any etiologic relationship between them and that infection. Indeed, such germs may not even be pathogenic for the patient, as I have repeatedly shown. Yet many autogenous vaccines are made up from just such organisms. Nor is the predominating germ necessarily the causal one in subacute and chronic infections, although many physicians and even some bacteriologists make their vaccine chiefly from it. Of 384 cultures made in Rosenow's brain broth, the predominating organism was capable of infecting the host in only 215 (56 per cent) and was nonpathogenic in 169 (44 per cent). The accompanying table shows the percentages for the different organisms. Moreover, in over 10 per cent of all the cultures in Rosenow's brain broth the infecting organisms failed to grow up.[15] This I have attributed to their being

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10. Proetz, A. W.: The Sinus in Perspective, Ann. Otol., Rhin. & Laryng. **38**: 682-684 (Sept.) 1929.

11. Carter, W. W.: A Plea for More Conservatism in the Treatment of Nasal Accessory Sinus Infections, Ann. Otol., Rhin. & Laryng. **39**: 578-583 (June) 1930.

12. Pond, C. W.: A Discussion of Some of the Clinical Problems of Chronic Sinusitis, Ann. Otol., Rhin. & Laryng. **37**: 677-690 (June) 1928.

13. Post, J. W.: Focal Infection of Alveolar Origin from the Standpoint of the Roentgenologist, Hahnemann Monthly **63**: 167-171 (March) 1930.

14. Billings, Frank: Focal Infection, p. 145.

15. Solis-Cohen, Myer, and Rubenstone, A. I.: The Technic of the Pathogen-Selective Method of Culture, J. Lab. & Clin. Med. **11**: 881-886 (June) 1926.

overgrown by the more numerous organisms that are nonpathogenic to the patient.[16] Is it to be wondered at, therefore, that vaccines so prepared often have little or no therapeutic effect?

For determining the causal organism in a subacute or chronic infection a number of methods have been devised, utilizing improved technic, differentiating mediums, animal passage, the bactericidal power of whole blood, tests for hypersensitiveness, and serologic tests, including agglutination, precipitation, hemolysin, absorption, complement fixation tests and the like. The pathogen-selective method is based on the assumption that organisms capable of growing in the fresh, whole, coagulable blood of the patient are those which are most pathogenic for that individual.[17] One of its advantages is that it furnishes a means for selecting the etiologically important organisms from a mixed culture. It is the only selective method described in Kolmer and Boerner's Approved Laboratory Technic.[18] Its simplicity makes it easily available for clinical use.

ERADICATING THE BACTERIAL FOCUS OF INFECTION BY MEANS OF VACCINE

In order to eradicate a bacterial focus of infection by stimulating resistance to the infecting bacteria and their toxins, the vaccine must contain all the infecting organisms.. This necessitates taking proper cultures of all possible foci, including the nasopharynx, which, as has been shown, may contain infecting organisms not present in the tonsils or in the tonsillar fossae. The vaccine, in my opinion, should contain as many antigens as possible, the soluble exotoxins as well as the endotoxins. Such a vaccine, however, is extremely potent and must be employed with great caution.

When the required specific antibodies have been produced in sufficient quantities to overcome the infecting organisms and their toxins, the focus of infection can truly be said to be eradicated at both the primary and the secondary foci.

CONCLUSIONS

1. The common conception of focal infection concentrates attention on the infected tissue rather than on the infecting bacteria.

2. When the physician speaks of eradicating a focus of infection, what he really means is removing infected tissue, such as tonsils or teeth, or draining and cleaning out an infected cavity, such as a nasal accessory sinus.

3. Infecting bacteria seldom are confined to a circumscribed area of diseased tissue but are present also on adjacent tissues, which may be apparently free from disease.

4. Enucleation of diseased tonsils does not necessarily remove the focus of infection, because the infecting organisms may still remain in tonsillar stumps, in recurring tonsillar tissue, in infratonsillar lymphoid tissue, and on the apparently normal mucous membrane of the tonsillar fossae and the nasopharynx.

5. A focus of infection in a nasal accessory sinus is not necessarily eliminated by treatment or operation, because infecting bacteria may still persist there.

6. Such expressions as "removal" or "elimination" or "eradication" of the focus of infection should be avoided when one is describing tonsillectomy or sinus treatment or operation.

7. The conception of focal infection should stress the bacterial element and regard the causal germ as the chief infecting agent.

8. Surgery alone cannot possibly remove all the infecting organisms, which can be overcome only by the patient's defensive forces.

9. The elimination of a focus of infection requires the production of bactericidins and other antibodies to destroy the infecting bacteria and render their toxins harmless, which can be aided by hygienic measures but in many cases needs the artificial stimulation of a potent vaccine containing the proper antigens obtained from the infecting bacteria.

10. The pathogen-selective culture selects the etiologically important organism from a mixed culture, and the vaccine made from it contains both the endotoxins and the soluble exotoxins of the infecting bacteria.

11. When, in addition to the extirpation of accessible and removable diseased tissue that has become a favorable soil for the propagation of the infecting germs, the required specific antibodies have been produced in sufficient quantities to overcome the infecting organisms and their toxins, the focus of infection can truly be said to be eradicated at both the primary and the secondary foci.

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16. Solis-Cohen (footnotes 6 and 8).
17. Solis-Cohen and Heist,[8] Boerner and Solis-Cohen,[6] Solis-Cohen and Rubenstone,[15] Solis-Cohen, Myer: Accentuating Pathogenic Organisms in Culture by Utilizing the Inhibitory Influence of Whole Blood, Brit. J. Exper. Path. **8**: 149-154 (June) 1927. Lowe, E. C.: Pathogen-Selective Cultures as an Aid to the Diagnosis of Infective Foci, Brit. M. J. **2**: 98-100 (July 21) 1928. Solis-Cohen, Myer: The Pathogen-Selective Vaccine: Its Preparation and Administration, M. Times **58**: 206-207 (July) 1930.
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EFFECT OF DIATHERMY TREATMENT OF KIDNEYS ON THE RENAL FUNCTION

AS MEASURED BY THE UREA CLEARANCE TEST

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Largely as the result of the speculation that Bright's disease results from spasm of the renal vessels, diathermy treatment has been extensively employed in this disease in the past few years. The belief has prevailed that the diathermy current actually heats the kidney and thus causes relaxation of the arteriolar spasm, in turn resulting in better perfusion of the kidney with blood.

Contradictory literature has grown up regarding the observed effects of renal diathermy.[1] Some investigators have found neither a diuretic effect nor any evident therapeutic advantage, whereas others have stated that they have had good results.

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1. These include:
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Bucky, G.: Anleitung zur Diathermiebehandlung, ed. 2, Vienna, Urban & Schwarzenberg, 1926.
Ewig, W.: Diathermiebehandlung der Nierenentzündung, Deutsche med. Wchnschr. **57**: 51 (Jan. 9) 1931.
Kolischer, G.: Diathermic Treatment of Medical Kidney Disease, Arch. Phys. Therapy **8**: 391 (Aug.) 1927.
Kowarschik, Josef: Die Diathermie, ed. 6, Berlin, Julius Springer, 1928.
McIntosh, J. F.; Möller, E., and Van Slyke, D. D.: Studies of Urea Excretion: III. The Influence of Body Size on Urea Output, J. Clin. Investigation **6**: 467 (Dec.) 1928.
Möller, E.; McIntosh, J. F., and Van Slyke, D. D.: Studies of Urea Excretion: II. Relationship Between Urine Volume and the Rate of Urea Excretion by Normal Adults, J. Clin. Investigation **6**: 427 (Dec.) 1928.
Nagelschmidt, Franz: Lehrbuch der Diathermie, ed. 3, Berlin, Julius Springer, 1926.
Rausch, Z.: Die Wirkung der Nierendiathermie auf die renalen Hypertonien, Deutsche med. Wchnschr. **58**: 1440 (Sept. 9) 1932.
Rautenberg: Die künstliche Durchwärmung innerer Organe, Deutsche Kong. f. inn. Med. **28**: 463, 1911.
Weinstein, M. L., and Klein, J.: The Effect of Medical Diathermy on the Renal Excretion of Urea and Chlorides, Illinois M. J. **51**: 385 (May) 1927.

In order to obtain evidence concerning the effects of diathermy on renal function I have observed the effect of one-hour periods of diathermy on the urea clearance. The subjects were either normal or those suffering from hemorrhagic Bright's disease, nephrosis, or essential hypertension.

PROCEDURE

The patients were all kept in bed during the test. A control period of one hour was run, followed by one hour of diathermy and again a one-hour control period. Four hundred cubic centimeters of water was given just before the collection of the first urine specimen and again before the diathermy was started. The blood urea was determined in the middle of each period. Before, during, and after the diathermy the urea clearance was estimated as described by Møller, McIntosh and Van Slyke.

Results of Diathermy

Case	Diagnosis	Blood Urea, Mg. per 100 Cc.	Corrected Urine Volume, Cc. per Minute*	Urea Clearance, per Cent of Normal		Blood Pressure: Systolic	Blood Pressure: Diastolic
1	Normal	16.5	2.5	80.7		116	70
		....	5.7	91.0	diathermy	112	72
		15.1	3.6	86.9			
2	Normal	13.5	6.5	112.0		122	80
		....	8.2	86.4	diathermy	114	76
		14.3	5.6	77.3			
3	Hemorrhagic Bright's disease	83.4	1.4	6.0		182	94
		....	2.7	7.1	diathermy	160	88
		81.3	2.4	6.9		164	88
4	Hemorrhagic Bright's disease	24.9	1.3	33.4			
		....	3.1	35.5	diathermy		
		24.5	3.0	28.8			
5	Hemorrhagic Bright's disease	26.5	1.0	92.0		120	78
		26.1	1.2	94.1	diathermy	118	76
		25.4	1.7	85.4			
6	Hemorrhagic Bright's disease	20.9	1.5	8.6		162	108
		....	2.2	8.6	diathermy	148	96
		20.5	2.7	12.5		152	98
		22.4	1.3	9.2		152	102
		22.2	1.9	9.5	diathermy	142	96
		22.5	2.0	9.7		130	96
7	Hemorrhagic Bright's disease	18.5	0.9	56.2			
		....	4.4	53.0	diathermy		
		17.9	6.5	53.5			
8	Hemorrhagic Bright's disease	62.6	1.1	15.4		160	110
		....	1.2	14.6	diathermy		
		62.3	1.3	14.9			
9	Hemorrhagic Bright's disease	75.9	1.3	14.3			
		....	1.9	13.9	diathermy		
		75.0	2.3	13.6			
10	Recovered hemorrhagic Bright's disease	12.0	4.6	95.3		140	82
		....	6.4	101.2	diathermy	142	66
		12.0	5.3	172.6		138	62
		10.9	2.9	121.8		124	62
		....	3.5	127.4	diathermy	120	60
		10.8	5.9	135.7			
11	Hemorrhagic Bright's disease	77.2	1.2	8.0		160	84
		77.6	1.9	7.0	diathermy	164	86
		76.4	2.2	7.7			
12	Essential hypertension	11.2	10.9	88.9		210	130
		11.0	7.9	80.5	diathermy	180	110
		9.6	10.3	111.7		184	116
		12.0	2.0	64.1		172	110
		11.9	4.6	94.8	diathermy	160	106
		11.4	11.8	80.3			
		11.2	10.9	88.9		184	116
		11.0	7.8	80.3	diathermy	188	112
13	Essential hypertension	7.5	6.6	65.2		288	136
		7.5	7.4	85.8	diathermy	248	126
		7.5	6.8	67.0			
		11.7	5.2	78.2		240	128
		10.8	6.9	80.7	diathermy	228	118
14	Malignant hypertension	18.9	0.6	64.5		240	140
		18.0	0.7	69.7	diathermy	234	140
		18.1	4.2	53.1			
		15.8	0.79	84.2		270	142
		16.2	0.95	98.7	diathermy	272	142
		16.0	3.4	60.9		280	146
		20.8	0.6	63.2		268	170
		....	1.0	65.6	diathermy	256	168
		20.5	1.1	59.0		262	170

* "Corrected urine volume" is the observed urine: Volume $\times \frac{1.73}{\text{sq. meters body surface}}$. The correction is used as described by McIntosh, Møller, and Van Slyke.

The diathermy machine employed was number 4 of the Westinghouse X-Ray Company. One electrode was placed over each kidney region and a large electrode over the upper part of the abdomen. An attempt was made to give as high dosage as could be tolerated by the patient without serious discomfort. In most cases from 1,700 to 1,900 milliamperes could be employed.

RESULTS

The accompanying table presents the results of the diathermy treatment.

In all cases the blood urea was not changed to any large extent, there being a slight tendency to fall from the first period to the last. Also, no consistent change in the water excretion was noted, and, lastly, the urea clearance was not altered significantly. Blood pressure measurements during the diathermy treatment showed no consistent change from the control level.

SUMMARY

Diathermy treatment has been given to fourteen subjects (normal subjects and patients with hemorrhagic Bright's disease, nephrosis and essential hypertension) for one-hour periods. No significant change was observed in the blood pressure or in the renal function as measured by the urea clearance test, diuresis or blood urea. The results afford no support for the assumption that renal diathermy is of therapeutic value in essential hypertension or Bright's disease.

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CREATINE METABOLISM IN CHILDREN WITH HYPOTHYROIDISM

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The discovery of metabolic functions of creatine in muscle metabolism has attracted considerable clinical interest in the study and treatment of disorders of the muscular system, particularly in pseudohypertrophic muscular dystrophy and myasthenia gravis. This subject was reviewed by Harris and Brand [1] in a recent issue of THE JOURNAL.

Evidence is gradually accumulating, however, which indicates that the metabolism of creatine has a wider clinical importance than in the specific myopathic diseases. Changes in creatine excretion have been noted in individuals not suffering from disorders of the muscular system. A detailed discussion of these changes and their significance in the various phases of normal and pathologic physiology may be found in the writings of Hunter [2] and Rose.[3] It seems likely that creatinuria in the human being is related to defective creatine storage in muscle or to abnormally high creatine synthesis. Creatinuria occurs in all types of muscular dystrophy and in states of increased endogenous protein catabolism, as in fever and in certain cases of

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1. Harris, M. M., and Brand, Erwin: Metabolic and Therapeutic Studies in the Myopathies, J. A. M. A. **101**:1047 (Sept. 30) 1933.
2. Hunter, Andrew: Monographs on Biochemistry, London, Longmans, Green & Company, 1928.
3. Rose, W. C.: Annual Review of Biochemistry **2**:187, 1933.

hyperthyroidism. Apparently a number of factors play a part in determining the extent of normal creatinuria, which in the present state of knowledge cannot be definitely interpreted.

Normally creatine is not found in the urine of the male adult, but small amounts of creatine are excreted periodically in the urine of normal women, possibly indicating a controlling influence of the sex hormones.[4] In infants and children, however, creatinuria is physiologic in both sexes until about the age of puberty. This fact was first pointed out by Rose[5] in 1911. Almost simultaneously, McCrudden[6] published the results of his investigations on the effect of carbohydrate and fat on the excretion of creatine in cases of retarded development. One of his subjects was a female cretin, aged 8 years, in whom creatine excretion was markedly reduced. The significance of this observation was not appreciated at the time, as there were meager data on creatine metabolism in pathologic conditions. However, some years later Beumer and Iseke[7] observed that hypothyroidism in children was invariably accompanied by a diminution and sometimes by a complete suppression of creatine excretion.[8] The same investigators also demonstrated that the creatine excretion in hypothyroid children returns to normal after the administration of thyroid extract. Since this observation, other investigators have noted an apparent relationship of creatine metabolism and thyroid activity.[9] Experimentally, it has been shown that operative removal of the thyroid gland leads to a reduction or complete cessation of creatine excretion and that it promptly returns to normal after the giving of thyroid extract.[10] It has also been shown that the thyrotropic hormone of the anterior pituitary lobe has almost the same effect as thyroid extract in producing an increased excretion of creatine in the normal adult rat.[11]

From these observations it appeared that the relationship of the creatine metabolism to thyroid activity might be of clinical interest. A number of clinical observations have been made in adults with severe hyperthyroidism when an increased creatine excretion has been found.[12] This information has limited clinical application for purposes of diagnosis, as the finding is not altogether consistent and as there are other more reliable diagnostic aids in that condition. In children, however, hypothyroidism often presents a difficult problem for diagnosis and treatment, particularly in borderline cases.

It seemed advisable, therefore, to investigate further the clinical significance of diminished thyroid activity and creatine metabolism during the period of childhood.

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6. McCrudden, F. H.: J. Exper. Med. **15**: 457, 1912.
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8. Scholz in 1905, while conducting a study of cretins, found creatinine excretion diminished but, owing to the methods used by the author, not much reliance can be placed on this observation.
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10. Schenk, P.: Arch. f. exper. Path. u. Pharmakol. **95**: 45, 1922. Frontali, G.: Arch. internat. Physiol. **12**: 431, 1924. Takahashi: Kongressblatt f. inn. Med. **43**: 751, 1921. Eimer, K.: Ztschr. f. d. ges. exper. Med. **77**: 455, 1931.
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12. Shaffer, P. A.: J. Biol. Chem. **31**: 1907; Proc. Am. Soc. Biol. Chem. XIII. Denis, W.: J. Biol. Chem. **29**: 447 (April), **30**: 47 (May) 1917. Kepler, E. J., and Boothby, W. M.: Am. J. M. Sc. **182**: 476 (Oct.) 1931. Brentano, C.: Arch. f. exper. Path. u. Pharmakol. **163**: 156, 1931. Hedrich, W.: Deutsches Arch. f. klin. Med. **171**: 27, 1931.

PROCEDURE AND METHODS

Extensive creatine and creatinine excretion studies have been carried out on thirty-four children, normal and with various types of pathologic conditions. Detailed observations are reported at this time on two cases of hypothyroidism in children. Twenty-four hour urine specimens were collected on two girls with hypothyroidism, one (D. J., aged 5 years) for fifty-three consecutive days and another (V. K., aged 12 years) for thirty-six consecutive days. The preformed creatinine was determined by the Folin colorimetric method and by the total creatinine by the Folin-Benedict method in duplicate. The patients were on a general hospital diet containing meat once a day and approximately a quart of milk a day.[13] Rectal temperatures were taken three times a day. As soon as the patients were stabilized metabolically, a creatine tolerance test was given consisting of 3 Gm. of creatine by mouth daily for seven days (D. J.) and five days (V. K.). The amount of creatine fed and eliminated is given in the charts. The periods in which thyroid extract was administered are indicated as to time and dosage.

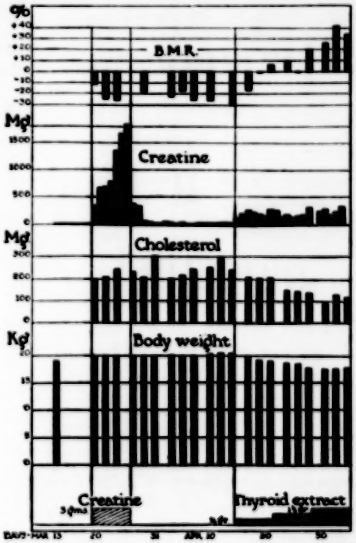

Chart 1.—Observations in the case of D. J., a girl, aged 5 years.

METABOLIC AND THERAPEUTIC OBSERVATIONS

The subjects showed an absence of the physiologic creatinuria of childhood when not receiving thyroid therapy or creatine by mouth. The absence of creatine from the urine was not due to a low protein intake, as the diet described was not creatine free and contained an adequate amount of protein. In the case of the older subject (V. K.), the experimental period was started while she was still on thyroid extract. This

13. The children were purposely not put on a weighed creatine-free diet as it was desired to study the creatine excretion under natural clinical conditions.

patient showed a gradual decrease in urinary creatine as the amount of thyroid extract administered was reduced. She continued to excrete creatine for three days after thyroid therapy was discontinued. Another hypothyroid child under observation showed the same reaction.

Creatine appeared in the urine the day following thyroid administration and continued as long as the thyroid extract was given. A temporary increase in creatine excretion was noted immediately following an increase in the dose of thyroid extract. The thyroid therapy had no appreciable effect on the preformed creatinine excretion. The total creatinine coefficient of the younger patient (D. J.) without treatment averaged 21.2. On thyroid treatment the average rose to 29.0. The first figure is lower and the latter figure higher

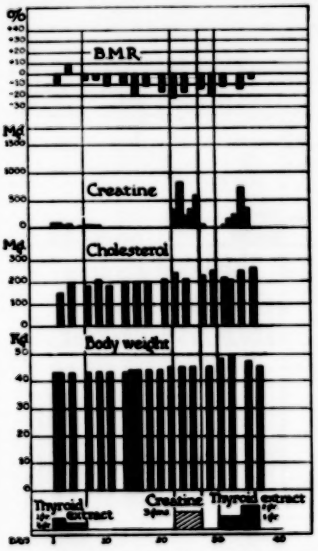

Chart 2.—Observations in the case of V. K., a girl, aged 12 years.

than the creatinine coefficient of 23, which is considered by Harding and Gaebler [14] to be normal for children. The older subject (V. K.) had an average total creatinine coefficient of 15.4 without treatment. On thyroid treatment the coefficient rose to 24.6.

The fate of ingested creatine in these cases is of interest. The younger child (D. J.) excreted only 45 per cent of the ingested creatine as creatine and showed no increase in creatinine excretion. This subject continued to excrete creatine in considerable quantities for four days after ingested creatine was discontinued. The older child (V. K.) excreted only 19 per cent of the ingested creatine but showed a definite rise in creatinine excretion. This patient excreted a small amount of creatine the day after creatine feeding was stopped, but it completely disappeared from the urine after the second day.

14. Harding, V. J., and Gaebler, O. H.: J. Biol. Chem. 54:579 (Nov.) 1922.

COMMENT

The hypothyroid children studied have shown a definite change in creatine metabolism. This is characterized by a diminution or complete absence of the physiologic creatinuria usually found in children up to the age of puberty. Thyroid feeding restores the hypothyroid child to the condition of creatinuria characteristic of the normal child. The creatinuria is seen to be a very delicate index of the effect of ingested thyroid, as it occurs even before any definite change is noted in the basal metabolism and blood cholesterol. It is not possible to state how the thyroid hormone affects the creatine metabolism, but it is obvious that directly or indirectly it exerts a profound and determining influence on the character of creatine metabolism. A probable explanation of the diminished creatine excretion is that it may be due to a low endogenous metabolism incident to hypothyroidism.

The response of the subjects to ingested creatine is also interesting. Both children have a greater tolerance for creatine than normal children of the same age. Krause [15] fed a considerably smaller quantity of creatine to two normal girls, one, aged 6 years, excreting creatine, and the other, aged 11 years, not excreting creatine. He found 56 per cent of the ingested creatine excreted in the case of the younger child and 31 per cent in the case of the older child.

Magee [16] studied two normal boys, aged 6 and 9 years, and found, respectively, 75 and 33 per cent of the endogenous creatine excreted as such. She also noted less conversion to creatinine and a more prolonged creatine excretion over a longer period of time in the younger child.

It has been found that with normal subjects the younger the child the relatively greater amount of both endogenous and exogenous creatine is excreted. In the two subjects studied there was an absence of endogenous creatine excretion during the period in which they were not receiving thyroid. When creatine was fed by mouth during the control period, the tolerance for creatine was found to be greater than in normal children and less appeared in the urine. Moreover, the normal tendency of the younger child to excrete more creatine on a creatine tolerance test is seen to be exhibited under conditions of hypothyroidism. In other words, while the quantitative response to the creatine tolerance test is modified by the condition of hypothyroidism, it has not altered the influence of age. The factors inherent in the age of the patient require further study.

The comparison of the changes in creatine excretion with other criteria of the efficacy of treatment in hypothyroidism is interesting. It will be noted from the charts that following thyroid therapy a change in creatine excretion takes place long before there is a significant change in the basal metabolic rate, blood cholesterol or body weight. From these observations it seems apparent that measurement of the urinary creatine is a delicate index of the effect of thyroid administration. In view of the greater ease, simplicity and reliability of creatine analysis than of the basal metabolic rate in children, it seems that this measurement may serve as a useful clinical aid in controlling thyroid medication.

15. Krause, R. A.: Quart. J. Exper. Physiol. 7:87-101, 1913.
16. Magee, M. Catherine: Creatine and Creatinine Metabolism in Progressive Muscular Dystrophy, Am. J. Dis. Child. 43:19 (Jan.) 1932.

SUMMARY AND CONCLUSIONS

1. The metabolism of creatine appears to be definitely influenced by thyroid activity during childhood.

2. During the period from infancy until about puberty, creatinuria is physiologic. Hypofunction of the thyroid causes a decrease or complete cessation of creatine excretion, which can be restored to normal values after the administration of thyroid extract. This is accompanied by a corresponding change in the clinical condition of the patient.

3. From a comparison with other diagnostic criteria of hypothyroidism in children, the change in creatine metabolism appears to be an important finding, which may be useful in diagnosis and in the control of therapy.

ENDEMIC TYPHUS FEVER IN HAWAII

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There is an ever increasing interest in the epidemiology and geographic distribution of American typhus fever.

Epidemic (Old World) typhus fever was well known to the physicians of the early nineteenth century. Typhus fever was first differentiated from typhoid by Gerhard, studying the Philadelphia epidemic of 1836. Typhoid means a disease like typhus fever. Typhus abdominalis became a clinical entity under the name of typhoid.

Eberth in 1880 and Gaffky in 1884 discovered the typhoid bacillus, now more properly designated Eberthella typhi.

Brill in 1897 observed a disease in New York, which he differentiated from typhoid and which, for a long time, bore his name. At that time he considered it a distinct clinical entity in no way related to typhoid, nor, later, to typhus fever. Subsequently it was proved to be immunologically similar to European typhus.

In 1906 Ricketts discovered the small gram-negative intracellular bodies that bear his name "Rickettsia" in the wood tick that transmits Rocky Mountain spotted fever, and these were later found in the human subjects of the disease, as well as in typhus fever subjects and typhus fever lice.

In 1909 Nicolle first succeeded in infecting monkeys with blood from typhus fever patients. Later it was demonstrated that in guinea-pigs the disease has a unique course.

In 1910 Wilson of Belfast and in 1914 Weil and Felix discovered that certain strains of B. proteus-vulgaris, isolated from the urine of typhus fever patients, were agglutinated in high dilution of blood from typhus fever patients. This is a heterologous agglutination, since the agglutinable strain of B. proteus-vulgaris, known as Proteus X 19, has no etiologic relationship to typhus fever. In low dilutions nonspecific agglutination may take place, but in dilutions over 1:300 it points quite diagnostically to typhus fever or Rocky Mountain spotted fever. This reaction, known as the Weil-Felix reaction, may become positive as early as the fifth day of the disease.

In 1931 Dyer and his associates conclusively proved that typhus fever (American variety, alias Brill's disease) was carried by the fleas of wild rats.

From the Clinic.

Most of the foregoing facts had been lost sight of by Honolulu physicians for, at irregular intervals during the past ten years, sporadic cases that clinically rather closely resembled typhoid have been reported as typhoid or paratyphoid in the face of consistently negative laboratory observations. Most of these cases were rather similar — a prodromal period, rather sudden onset, rose spots of exaggerated character on the chest, abdomen, inner arms and thighs (but not on the wrists, ankles or face), headache, cough, fever as high as 104 F., a spleen normal in size, no enteric symptoms save frequently constipation, sterile blood cultures, stool cultures negative for the typhoid group (occasionally a bacillus suspected of being paratyphoid C)—afebrile a bit too early for typhoid, negative Widal reaction and negative agglutination reaction for Alcaligenes abortus, Alcaligenes melitensis and the bacillus of tularemia. The laboratories received undeserved criticism. The clinician and the clinical pathologist were making the same mistake again and again and calling it experience.

Almost a hundred years after Gerhard differentiated typhoid from epidemic typhus fever the physicians of Honolulu were faced with the need to differentiate endemic typhus fever from typhoid. McCoy of the National Institute of Public Health, here to investigate leprosy in August 1932, suggested that this atypical symptom complex might belong in the group of Rickettsia or typhus-like diseases. He was good enough to send us subcultures of Proteus X 19.

Not until recently did an opportunity to investigate a typical case present itself:

Mrs. S. became suddenly ill with headache, malaise and body pains, Sept. 2, 1933. September 23 she was again afebrile and convalescent. During the three weeks of her illness she presented the characteristic manifestations of headache, malaise, constipation and later loose bowels, typically exaggerated maculopapular "rose spots," no splenic enlargement, fever to 104 F., negative blood and oft repeated feces cultures, and negative agglutination reactions, even after convalescence, with B. typhosus, paratyphoid A and B, and Alcaligenes abortus, Alcaligenes melitensis and the bacillus of tularemia. There were no complications nor sequelae.

October 9, the blood serum, in a dilution as high as 1:10,000, gave an easily read agglutination of Proteus X 19, a twenty-four hour culture being used, suspended in saline solution and incubated two hours at 37 C. and in the icebox over night. Control serums did not agglutinate in dilutions of 1:320, though some were positive in 1:160. This seemed to offer conclusive proof that the patient had been suffering from endemic typhus fever, since the symptomatology ruled out epidemic typhus fever as well as Rocky Mountain spotted fever, both of the Western and Eastern type.

Just previous to the inception of her illness the patient had moved into a newly constructed house the yard of which had served as a trash dump for neighbors during the construction, affording an excellent rat harborage.

I investigated with the Weil-Felix reaction a series of patients sick two years previously. In the H. family of three, the father had first become ill with the symptoms of an atypical typhoid. The father had hardly entered convalescence when the young son contracted the same disease. Shortly after that the mother became ill with the same symptoms, excepting that in her case the rose-macular rash was very prominent. All three patients made rather rapid recoveries. Two years after the illness the serum of the father agglutinated Proteus X 19 in a dilution of 1:320, the son's in 1:640 and the mother's in 1:1,280. At the time of their illness many laboratory procedures had been instituted in their cases, as well as in the case of a maid, suspected of being a typhoid carrier, in an effort to confirm the diagnosis of typhoid, all to no avail. At the time of their illness, this family had had in their home a small

colony of white rats, as pets, whose cage was accessible to wild rats. The female white rat was sick at that time and for that reason the colony was given away just after Mrs. H.'s illness.

A further survey showed that three other patients, leaving the hospital just recently with a diagnosis of fever of undetermined origin, gave strong Weil-Felix reactions, one in a dilution of 1:5,000, another in 1:10,000. Another patient, Miss M., ill at that time in the hospital with typical symptomatology, but admitted with a provisional diagnosis of typhoid or measles, on or about the seventeenth day of the disease gave a Weil-Felix reaction in a dilution of 1:80,000.

At the present writing about ten cases have been detected in Honolulu. These facts were presented before the Honolulu County Medical Society, Nov. 3, 1933, and it is anticipated that more cases will now come to light. Honolulu has recently been through a prolonged spell of very dry weather, excellent for the breeding of rat fleas, and the present high incidence of endemic typhus fever may be dependent on that fact.

Three cases of unconfirmed typhoid of from one to two years ago failed to give any agglutination with Proteus X 19; not all unconfirmed typhoid is necessarily typhus fever.

The older writings, in a confused fashion, tell of epidemics of typhus fever in the Sandwich Islands; certainly there has been no Old World typhus fever here since 1898. Just what the interepidemic reservoir of Old World typhus fever is seems to be still a mystery. This disease, transmitted from man to louse to man, might outlive the interepidemic period in man in an attenuated, afebrile form, but no proof of this has been advanced. The louse does not transmit the disease to the nit or to the next generation.

Endemic typhus fever is to be found chiefly on the Atlantic and Gulf seaboard, from the North, well into the South, and as far inland as Montgomery, Ala. A focus in and around Savannah, Ga., seems to have been closely studied; under observation, Dr. V. H. Bassett says its mortality is certainly increasing. While the mortality is usually given as 1 per cent, there has been one death for each twelve cases in the course of a certain year.

As far as I can determine, no cases have been reported from the inland part of the United States, from the Middle West or from the Far West. Cases have been reported from southern California and from several other points within the continental part of the United States, but there is reason to believe that these were imported cases of Mexican Tabardillo fever, more akin to Old World typhus fever in its mode of transmission and mortality. If, in the Middle and Far West, every case of fever of unconfirmed origin should be given the benefit of a Weil-Felix reaction in addition to the Widal, it is possible that new foci of the disease might be discovered.

While epidemic typhus fever is a disease of man, transmitted from man to man by the louse, endemic typhus fever is essentially a disease of rats, transmitted to the flea and then, by accident, transmitted to man. Here the passage ceases; the quarantine regulations should be aimed at the rats, not the patient. It has been proved that rats from an area in which human cases of endemic typhus fever have arisen carry in their brains and suprarenals the virus of the disease.

Epidemic typhus fever is a disease of winter, endemic typhus fever one of summer and fall. The time of greatest prevalence of lice is winter; that of fleas is summer and fall. Fortunately, in the East, the prevalence periods of these two vectors do not much overlap. Even in the southern part of the United States there are seasonal changes.

Here in Hawaii, however, temperature and seasonal fluctuations are practically nil; almost any month of the calendar may be the hottest, the coldest, the wettest or the dryest. Of rat fleas there are plenty; fortunately there are not many lice, but they do exist. And now there is reason to believe that there is an endemic typhus fever reservoir in our rats. With this marked overlap of vector seasons, it will be interesting to see whether some day unwittingly the experiment of passing the virus of endemic typhus fever may be performed from a rat to a flea, and from that flea to a louse-infested man, and from that man to a louse, and from that louse to a second man. What will the second man have, endemic typhus fever or epidemic typhus fever?

On two of our islands, Hawaii and Maui, there exist limited areas in which the rat population is infected with plague bacillus and in which areas occasional human cases appear. There is at present being conducted, through cooperation of the federal and territorial governments, an intensive epidemiologic survey of the rat and flea situation, from the plague point of view. This machinery, already set up, might with little additional expense and labor investigate the same rats and fleas for the presence of endemic typhus fever. It is obvious that further cross protection experiments in guinea-pigs, with the viruses of typhus fever, epidemic and endemic, and spotted fever, Eastern and Western, must be carried out against the local infection. The local material must come from human patients, rat fleas and rat tissues. At present the mentioned stock strains of viruses are not available in the territory.[1]

The established presence of endemic typhus fever in Honolulu should be of considerable interest not only to the local health authorities but also to those of Seattle, San Francisco and Los Angeles, as well as to those of Japan, China and the Philippines. With the ever decreasing time of transport from one of these places to the other, the danger of disseminating this disease increases. While rat guards are placed about shipping with meticulous care, there is always danger of a break in technic. At present, with its three weeks of illness and a very low mortality rate, this disease has a greater economic importance than one of public health. But who is to say, with accuracy, what our peculiar geographic location plus our peculiar climatic conditions may mean to the natural history of this disease?

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1. Since the foregoing was written, serum from one of the reported cases was submitted to the U. S. Public Health Service and protection tests were carried out at the National Institute of Health, through the courtesy of that bureau. Of six control pigs inoculated with typhus virus only, all developed characteristic fever and scrotal lesions; all six pigs inoculated with this virus plus 0.5 cc. of convalescents' serum failed to develop characteristic fevers and scrotal lesions. This makes the diagnosis of endemic typhus highly presumptive.

Ketosis.—Under conditions of starvation, or the administration of a diet low in carbohydrate and high in fat, or in diabetes in which the carbohydrate metabolism is perverted, keto-acids are produced in the body. These acids appear in the blood and are excreted into the urine by the kidneys as aceto-acetic acid and β-hydroxybutyric acid, the latter being produced apparently by reduction of the former. The acetone excreted is formed by the decomposition of these acids. This condition of ketosis arises from the failure of oxidation of the fatty acids with an even number of carbon atoms beyond the point where the chain is reduced to the four carbon acids above mentioned. —Gainsborough, Hugh: The Therapeutic Use of the Ketogenic Diet, *Practitioner* **132**:45 (Jan.) 1934.

SEVERE GRANULOPENIA FOLLOWING THE USE OF BARBITURATES AND AMIDOPYRINE

REPORT OF A CASE

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KANSAS CITY, MO.

Following Schulz's classic description of agranulocytic angina in 1922, reports of an apparently primary type of leukopenia have become increasingly numerous. According to the recent statement of Madison and Squier,[1] over 500 of these cases are now on record. Wells [2] has quoted Stursberg, Marchand and Blumer as stating that differentiation during life between overwhelming sepsis, so-called aleukemic leukemia and agranulocytosis may at times be impossible. With this in mind it would be helpful to call these cases granulopenia. Kracke [3] has suggested this term because it places emphasis on the one common observation and accurately describes the characteristic blood picture. Obviously, much would be gained if these conditions could be classified according to the etiology involved.

It has long been recognized that benzene is highly toxic to the bone marrow, and benzene poisoning has been extensively studied both clinically and experimentally. It has only recently been suggested, however, that the enormous number of drugs containing a benzene chain might be a source of benzene intoxication. Emile-Weil [4] recently pointed out that the incidence of benzene poisoning has been increasing parallel with the increasing use of benzene in industry. Likewise, it may be significant that the apparent increase in the incidence of granulocytic leukopenia parallels the increasing use of such benzene derivatives as the barbiturates and amidopyrine.

The following case is presented because it adds to the evidence suggesting that severe granulopenia may follow from the combined administration of such commonly used drugs as Luminal and Pyramidon.

REPORT OF CASE

A woman house physician, aged 25, had been previously in good health. Oct. 31, 1933, because of headache, she took amidopyrine (Pyramidon), 5 grains (0.3 Gm.), and phenobarbital (Luminal), one-half grain (0.03 Gm.), at 1 p. m. During the afternoon she felt as though she was "coming down with a cold" and complained of continued headache, malaise and chilliness. Her temperature, first taken at 5 p. m., was 101, and she went to bed at that time. At 7 p. m. she took allylisopropylbarbituric acid (Alurate), 2 grains (0.13 Gm.), and one tablet of Lumodrin, the latter containing, according to the label, Ephedrin hydrochlorid, gr. ½; Luminal, gr. ¼; Pyramidon, gr. 2. At 8 p. m. she suffered a severe shaking chill and was moved into isolation quarters. Her fever at 10 p. m. was 103 and the pulse rate was 120. Physical examination was otherwise entirely negative. The next morning the laboratory found the hemoglobin to be 71 per cent, the red cell count 3,820,000, and the white cell count 2,950, with 51 per cent of polymorphonuclear neutrophils. Three hours later the total white count was unchanged, but 10 per cent of immature neutrophils were noted. At 4 p. m. the white cell count was 2,050, with only 30 per cent of granulocytic cells, 17 per cent of which were myelocytes. During the next two days the total white count remained practically unchanged but the differential counts showed a slowly increasing percentage of mature granulocytes. Blood films were examined repeatedly for malaria but nothing suggestive was seen. The urine was normal. On the fourth day the white count was 2,900, with only 3 per cent of immature granulocytic cells. Except for continued weakness the patient felt practically normal. On the fifth day she returned to duty, feeling stronger but with a white count still under 4,000 and a differential count at times showing myelocytes and many band forms. Several days later, when the possibility was realized that the drugs used might have been responsible for the chill and leukopenia, the following additional interesting history was obtained:

The patient had been quite certain that she had not previously used either barbiturates or amidopyrine except on one other occasion, and that almost a year before. At that time, the onset of a week's illness had also been preceded by an afternoon headache. She had then likewise taken amidopyrine and phenobarbital for relief. A few hours later she had suffered a chill and afterward remained in bed several days on account of weakness. Her condition had at that time been regarded as a case of influenza, but no blood counts had been taken on that occasion.

It was practically six weeks before a normal differential count was recorded, when the total count was 7,000. Except immediately after the initial chill, her temperature has been normal. This fact, together with absence of palpable glands or spleen, and so uneventful and complete a clinical recovery, appears to rule out everything except a transitory leukopenia.

I have recently attempted to evaluate the allergic factor in this patient's reaction to phenobarbital and amidopyrine by injecting, subcutaneously, small amounts of each drug, both separately and combined, in saline solution. The local reactions were slight and seemed to indicate no hypersensitiveness to the benzene chain as far as the patient's skin was concerned. Likewise, no appreciable change was noted in the leukocyte count following the injection of such small amounts of these drugs.

COMMENT

In 1931 Kracke [5] reported severe and repeated attacks of agranulocytosis in an individual using large amounts of coal tar derivatives. At that time he suggested that the benzene chain contained in these drugs might act as a powerful leukocytic depressant. More recently he [6] has reported that a review of nine cases of agranulocytosis revealed that eight of these individuals had been taking benzene derivatives prior to the clinical onset of their illness.

It is the commonly accepted belief that the reacting power of the individual's bone marrow determines the type and effectiveness of all leukocytic response. This fact serves to emphasize the seriousness of employing drugs that may be capable of depressing the mechanism of leukocytosis. It seems only a matter of wisdom, in the light of recent observations, to regard the use of barbiturates and amidopyrine with this possibility in mind. Available evidence is hardly sufficient to contraindicate entirely the use of these drugs, but their administration calls for watchful supervision on the part of both the clinician and the laboratory.

SUMMARY

Granulopenia should not be regarded as a primary type of blood dyscrasia until all possible etiologic factors have been eliminated.

An apparent increase in the occurrence of granulopenia may be related to the widespread use of drugs containing a benzene derivative.

A woman, aged 25, developed an acute and alarming leukopenia following the use of barbiturates and amidopyrine for the relief of a simple headache.

From the Department of Pathology St. Luke's and Children's Mercy Hospitals.

1. Madison, F. W., and Squier, T. L.: Primary Granulocytopenia After Administration of Benzene Chain Derivatives, abstr. J. A. M. A. **101**: 2024 (Dec. 23) 1933. S. B. Grant, P. S. Hench, Johnson McGuire and C. H. Watkins in the discussion, and personal communications to the author.
2. Wells, A. H.: J. Missouri M. A. **30**: 237 (June) 1933.
3. Kracke, R. R.: J. Lab. & Clin. Med. **17**: 993 (July) 1932; U. S. Nav. M. Bull. **30**: 16 (Jan.) 1932.
4. Emile-Weil, P.: Hemopathies Due to Benzene, Paris méd. **2**: 112 (Aug. 5) 1933; abstr. J. A. M. A. **101**: 1276 (Oct. 14) 1933.
5. Kracke, R. R.: Am. J. Clin. Path. **1**: 385 (Sept.) 1931.
6. Kracke, R. R.: Am. J. Clin. Path. **2**: 11 (Jan) 1932.

The benzene chain contained in both drugs is possibly responsible for the severe reaction and the disappearance of the granulocytes from the blood.

A number of similar cases have been reported recently.

A difference may be expected in the reaction to benzene quickly absorbed from the alimentary tract, as compared to the type of benzene poisoning that may result from the prolonged, slow absorption that occurs in industrial exposure.

Individuals are known to vary greatly in their susceptibility to benzene. Granulopenia following the use of barbiturates and amidopyrine may therefore occur only in those individuals who are unusually susceptible to the benzene chain.

Forty-Fourth and Mill Creek Parkway.

CLINICAL MANIFESTATIONS OF HIGH AND LOW PLASMA MAGNESIUM

DANGERS OF EPSOM SALT PURGATION IN NEPHRITIS

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Although a great deal of clinical significance has been attached to variations in blood calcium, variations in blood magnesium have entirely escaped notice. Very little has been known even about what happens when a patient takes an ordinary purgative dose of epsom salt. Matthew Hay [1] found that one normal man excreted 28 per cent of the ingested magnesium through the kidneys in twenty-four hours, and Yvon [2] found 21 per cent. Using a new and convenient method for the quantitative determination of magnesium in blood plasma and urine, we [3] have found that seven normal men excreted from 40 to 44 per cent (average 42.6 per cent) of the magnesium taken in a single ordinary purgative dose of epsom salt within twenty-four hours after ingestion. However, in spite of the large amount of magnesium absorbed, the concentration of magnesium in the blood plasma (normal, from 1.8 to 2.5 mg. of magnesium per hundred cubic centimeters; average normal, 2.09) is scarcely affected (average increase, 0.24 mg. of magnesium per hundred cubic centimeters; maximum increase, 0.41 mg.). In normal dogs and normal rabbits the percentage of ingested magnesium that is excreted and the concentration of the magnesium in the blood plasma are almost exactly the same as in man, and with corresponding doses by mouth the plasma concentration also remains practically unchanged. In animals the percentage of the ingested magnesium that is excreted in the urine is practically constant, regardless of the dose ingested or of the concentration of magnesium in the blood plasma.

From the Department of Pharmacology, University of Minnesota.

This paper was announced for presentation before the Section on Pharmacology and Therapeutics of the American Medical Association at the Milwaukee Session, June 15, 1933.

This investigation was made possible by a grant of funds from the Therapeutic Research Committee of the American Medical Association. Most of the patients on whom the observations were made were in the medical service of Dr. Hobart A. Reimann at the University of Minnesota Hospital and of Dr. George E. Fahr at the Minneapolis General Hospital. One was from the private practice of Dr. Charles B. Wright and three from the neurologic service of Dr. Joseph C. Michael at the Minneapolis General Hospital, all of whose cooperation is deeply appreciated. Preliminary reports have been published in Proceedings of the American Society for Clinical Investigation (J. Clin. Investigation **11**: 841 [July] 1932; **12**: 983, 1933), Proceedings of the American Society for Pharmacology and Experimental Therapeutics (J. Pharmacol. & Exper. Therap. **48**: 277, 1933) and Proceedings of the Society for Experimental Biology and Medicine (Proc. Soc. Exper. Biol. & Med. **30**: 996, 1933).

1. Hay, Matthew: J. Anat. & Physiol. **17**: 222, 1883.
2. Yvon, P.: Arch. de physiol. norm. et path. **5**: 304, 1898.
3. Hirschfelder, A. D., and Serles, E. R.: J. Clin. Investigation **11**: 841 (July) 1932; J. Biol. Chem., March, 1934.

HIGH PLASMA MAGNESIUM (HYPERMAGNESEMIA) AND EPSOM SALT PURGATION

However, when the kidneys are injured, the results are totally different. We have found in animals in which renal injury had been produced experimentally that less magnesium is excreted than normally. The excretion of magnesium is less in animals in which the tubules are more severely injured than the glomeruli (corrosive mercuric chloride nephrosis) than in those in which the glomeruli are injured more than the tubules (cantharides glomerulonephritis). The decrease in excretion of magnesium corresponds quite closely to the decrease in excretion of phenolsulphonphthalein but does not correspond to the alterations in excretion of xylose. We have found also that in nephrectomized animals and in animals with renal, and especially tubular, insufficiency the ingestion of magnesium sulphate causes a tremendous and rapid rise in plasma magnesium, sufficient even to bring them into a state of coma. Coma occurred whenever the plasma calcium reached or exceeded 17 mg. of magnesium per hundred cubic centimeters of plasma. This exactly coincides with the level at which Neuwirth and Wallace [4] and Taylor and Winter [5] found coma setting in after the subcutaneous injection of magnesium salts.

We have therefore studied the effects of the ingestion of ordinary purgative doses of magnesium sulphate on the plasma magnesium and the general physical condition in a series of patients suffering from renal disease. In all these patients, just as in the nephritic animals, a tremendous rise in plasma magnesium occurred within from four to six hours after an ordinary purgative dose of magnesium sulphate (epsom salt) had been taken by mouth. While one such dose was not sufficient to raise the magnesium concentration in the plasma to the level at which coma sets in (about 17 mg. of magnesium per hundred cubic centimeters of plasma), it often did rise to about two thirds of that concentration (from 9 to 11 mg.) and a number of the patients did show a decidedly increased drowsiness or even a light coma accompanying the increase in plasma magnesium. The results are indicated in chart 1.

NOTES ON CASES

Normal.—Plasma: [6] nonprotein nitrogen, 30 mg.; creatinine, from 1.5 to 2.0 mg.; magnesium, from 1.85 to 2.09 mg. After taking from 20 to 30 Gm. of epsom salt ($MgSO_4.7H_2O$): average increase, 0.24 mg.; maximum increase, 0.4 mg. Excreted in urine: phenolsulphonphthalein, from 60 to 80 per cent in two hours; magnesium excreted in twenty-four hours, from 40 to 44 per cent (average 42.6 per cent) of the magnesium ingested.

HIGH PLASMA MAGNESIUM

CASE 1.—*Subacute glomerulonephritis.* W. A., a woman, aged 41, in the Minneapolis General Hospital, complained of edema. Plasma: nonprotein nitrogen, 88; creatinine, 5.5; magnesium, 2.98; calcium, 11.3. Urine: phenolsulphonphthalein, 39 per cent. After 25 Gm. of epsom salt by mouth: Plasma: magnesium, 5.5; calcium, 13.0. Magnesium excreted in twenty-four hours: 23.8 per cent. Little effect on mental activity.

4. Neuwirth, I., and Wallace, G. B.: J. Pharmacol. & Exper. Therap. **35**: 171 (Feb.) 1929.
5. Taylor, W. F., and Winter, J. E.: J. Pharmacol. & Exper. Therap. **35**: 435 (April) 1929.
6. Amounts in plasma are always milligrams per hundred cubic centimeters.

CASE 2.—*Nephrosis.* L., a woman, aged 25, in the Minneapolis General Hospital, was mentally alert. Plasma: nonprotein nitrogen, 73; creatinine, 4.7; magnesium, 2.98; calcium, 11.3. Urine: phenolsulphonphthalein, 29 per cent. Mentally active. After 20 Gm. of epsom salt by mouth: Plasma: magnesium, 7.75; calcium, 14.9. Urine: magnesium excreted, 21.7 per cent. Listless and drowsy.

CASE 3.—*Acute glomerulonephritis.* M. R., a man, aged 33, in the University Hospital, with a blood pressure of 150 systolic, 100 diastolic, was mentally alert. Plasma: nonprotein nitrogen, 60; creatinine, 4.9; magnesium, 1.87; calcium, 9.8. Urine: albumin + + ; phenolsulphonphthalein, 39 per cent. After 30 Gm. of epsom salt by mouth: Plasma: magnesium, 7.9; calcium, 14.8. Urine: magnesium excreted, 26.3 per cent. Near coma, vomiting.

CASE 4.—*Acute glomerulonephritis.* K., a woman, aged 57, in the Minneapolis General Hospital, with a blood pressure of 170 systolic, 115 diastolic, was mentally active. Plasma: nonprotein nitrogen 98; creatinine, 8.9; magnesium, 2.73; calcium, 11.9. Urine: albumin + + + ; phenolsulphonphthalein, 59 per cent. After 20 Gm. of epsom salt by mouth: Plasma: magnesium, 9.22; calcium, 15.7. Urine: magnesium, 20.7 per cent. Very drowsy, near coma.

CASE 5.—*Chronic glomerulonephritis.* L. J., a woman, aged 35, in the University Hospital, was inactive and drowsy. Plasma: nonprotein nitrogen, 136; creatinine, 12; magnesium, 3.9; calcium, 19.9. Urine: albumin + + + ; phenolsulphonphthalein, 26 per cent. After 25 Gm. of epsom salt by mouth: Plasma: nonprotein nitrogen, 136; creatinine, 12; magnesium, 16.5 per cent. Light coma.

CASE 6.—*Chronic glomerulonephritis.* R. A., a man, aged 60, in the Minneapolis General Hospital, with a blood pressure of 190 systolic, 125 diastolic, was mentally alert. Plasma: nonprotein nitrogen, 185; creatinine, 17.5; magnesium, 4.78; calcium, 15.2. Urine: albumin + + + + ; phenolsulphonphthalein, 15 per cent. After 25 Gm. of epsom salt: Plasma: magnesium, 10.35; calcium, 23.5. Urine: magnesium, 10 per cent. Light coma, hard to awaken.

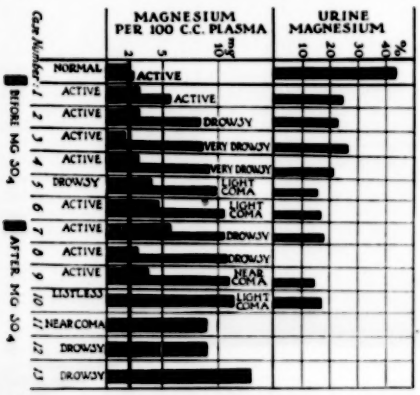

Chart 1.—Observations in cases showing high plasma magnesium: Urine magnesium = percentage of ingested magnesium excreted in urine in twenty-four hours. Before magnesium sulphate = milligrams of magnesium per hundred cubic centimeters of plasma before taking epsom salt ($MgSO_4 \cdot 7H_2O$) by mouth. After magnesium = milligrams of magnesium per hundred cubic centimeters of plasma from four to six hours after taking epsom salt by mouth. Words below the cross-hatched lines refer to mental condition before taking epsom salt; those above the solid line represent mental condition from four to six hours after taking epsom salt.

CASE 7.—*Acute glomerulonephritis.* E. P., a man, aged 43, in the Minneapolis General Hospital, with a blood pressure of 165 systolic, 110 diastolic, was mentally alert. Plasma: nonprotein nitrogen, 85; creatinine, 8.75; magnesium, 5.75; calcium, 19.75. Urine: albumin + + + ; phenolsulphonphthalein, 15 per cent. After 30 Gm. of epsom salt by mouth: Plasma: magnesium, 10.5; calcium, 24.1. Urine: magnesium, 18.5 per cent. Very drowsy.

CASE 8.—*Acute glomerulonephritis.* E. R., a woman, aged 39, in the University Hospital, with a blood pressure of 150 systolic, 110 diastolic, was very alert. Plasma: nonprotein nitrogen, 100;

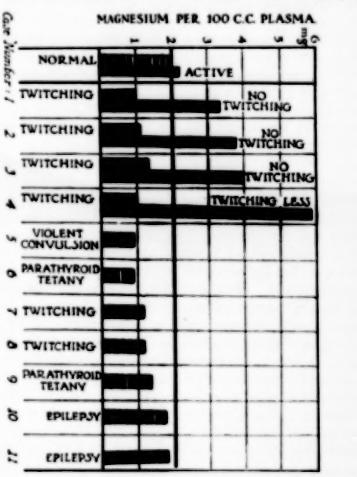

Chart 2.—Observations in cases showing low plasma magnesium. Legends have same significance as in chart 1.

creatinine, 9; magnesium, 2.49; calcium, 11.0. Urine: albumin + + + ; phenolsulphonphthalein, 27.5 per cent. After 30 Gm. of epsom salt: Plasma: magnesium, 10.75; calcium, 17.8. Drowsy.

CASE 9.—*Chronic glomerulonephritis.* E. L., a woman, aged 27, in the University Hospital, with a blood pressure of 200 systolic, 135 diastolic, was alert. Plasma: nonprotein nitrogen, 265; creatinine, 23; magnesium, 4.1; calcium, 16.9. Urine: albumin + + + + ; phenolsulphonphthalein, 12 per cent. After 20 Gm. of epsom salt by mouth: Plasma: magnesium, 10.91; calcium, 18.5. Urine: magnesium, 15.35. Very drowsy, difficult to awaken.

CASE 10.—*Acute glomerulonephritis.* O. L., a man, aged 58, in the University Hospital, with a blood pressure of 185 systolic, 140 diastolic, was listless. Plasma: nonprotein nitrogen, 195.5; creatinine, 25.3; magnesium, 4.25; calcium, 19.5. Urine: albumin + + + ; phenolsulphonphthalein, 12 per cent. After 30 Gm. of epsom salt by mouth: Plasma: magnesium, 11.32; calcium, 25.9. Urine: magnesium, 17.5 per cent. Hard to awaken, light coma.

CASE 11.—*Chronic glomerulonephritis.* J. J., a woman, aged 62, in the University Hospital, with a blood pressure of 175 systolic, 125 diastolic, near coma. Plasma: nonprotein nitrogen, 215; creatinine, 25; magnesium, 8.93; calcium, 19.7. Urine: albumin + + + ; phenolsulphonphthalein, 12.8. No epsom salt given.

CASE 12.—*Subacute glomerulonephritis.* O. J., a woman, aged 31, in the University Hospital, was very dull and listless. Plasma: nonprotein nitrogen, 190; creatinine, 22; magnesium, 9.0; calcium, 24.0. Urine: albumin + + + + ; phenolsulphonphthalein, 17 per cent.

CASE 13.—*Acute glomerulonephritis.* F. S., a man, aged 52, in the University Hospital, with a blood pressure of 190 systolic, 115 diastolic, was very drowsy. Plasma: nonprotein nitrogen, 190; creatinine, 21.5; magnesium, 13.0; calcium, 22.0. Urine: albumin + + + + ; phenolsulphonphthalein, 5 per cent; total urine, 150 cc. Died. Autopsy showed arteriosclerotic kidneys.

Since a single ordinary dose of epsom salt by mouth can raise the concentration of magnesium in the blood of nephritic patients to two thirds of the concentration at which coma sets in and since with larger doses it is easy to induce coma in nephritic animals, it seems probable that a few repeated doses of epsom salt would induce coma in the patients. It is therefore most probable that there are every year in the United States many hundreds of cases of coma occurring in nephritic patients which are diagnosed uremic coma but which in reality are magnesium coma caused by the use of epsom salt as a purgative. Since experimental animals could be brought out of this coma instantly and their lives could be prolonged by the intravenous injection of calcium chloride, the intravenous injection of calcium chloride would probably restore such patients to consciousness.

We are not stating, nor do we think, that all or even most cases of uremic coma are due to magnesium intoxication, but we are merely calling attention to the fact that a condition of coma easily mistaken for uremic coma can be induced in nephritic patients by epsom salt purgation. Magnesium citrate would unquestionably have the same effect.

Our results in no way contradict those of Blackfan and his collaborators,[7] who have administered magnesium sulphate intravenously for the control of uremic convulsions, or those of Dorsett[8] and McNeile and Vruwink[9] for eclamptic convulsions. Since they gave intravenously in carefully controlled doses only sufficient magnesium sulphate to produce subsidence of the convulsions, they stopped the administration as soon as a sufficiently high level of magnesium concentration in the blood had been reached. However, when the drug is administered by mouth and absorbed continuously from the intestine without regard to its concentration in the blood, this level can easily be exceeded.

Since our experiments on animals with renal insufficiency have shown that coma cannot be induced by tremendous doses of sodium sulphate, it would appear that sodium sulphate should be the saline purgative of choice in patients with renal disease.

Our experiments on animals[10] showed also that animals whose plasma magnesium was only slightly raised (to 5 mg. or more) were much more sensitive than normal animals to ordinary doses of morphine.[7] This explains Dr. Osler's old aphorism that "in severe nephritics and very old persons morphine should be given with caution." Epsom salt was Dr. Osler's favorite saline purgative and was administered almost as a routine in his wards at Johns Hopkins Hospital.

LOW PLASMA MAGNESIUM (HYPOMAGNESEMIA)

Since Kruse, Orent and McCollum[11] have induced a form of tetany in rats that were raised on a diet free from magnesium, it seemed probable that cases showing convulsions or other conditions of increased neuromuscular activity would be encountered clinically in which the plasma magnesium is low.

We have encountered thus far ten such clinical cases, in each of which convulsions or muscular twitchings were present. The data of these cases are shown in chart 2.

Case 14.—*Chronic glomerulonephritis, hypertension and convulsions.* S., a woman, aged 53, at the University Hospital, complained of edema of the legs and arms, and of intermittent general muscular twitchings. Plasma: nonprotein nitrogen, 200; creatinine, 15; magnesium, 0.95; calcium, 10.8. Urine: albumin +++; phenolsulphonphthalein, 12 per cent. After 20 Gm. of epsom salt by mouth: Plasma: magnesium, 3.3; calcium 11.9. No more twitching.

Case 15.—*Chronic glomerulonephritis.* C. O., a man, aged 36, in the Swedish Hospital, had general muscular twitching. Plasma: nonprotein nitrogen, 76.5; creatinine, 5.5; magnesium, 1.09; calcium, 9.3. Urine: albumin ++; phenolsulphonphthalein, 22 per cent. After 20 Gm. of epsom salt by mouth: Plasma: magnesium, 3.78; calcium, 13.0. No twitching.

Case 16.—*Chronic glomerulonephritis.* P. S., a man, aged 51, at the Minneapolis General Hospital, was nervous, and had general muscular twitching. Plasma: nonprotein nitrogen, 55.0; creatinine, 4.3; magnesium, 1.31; calcium, 16.7. Urine: albumin ++; phenolsulphonphthalein, 33 per cent. After 25 Gm. of epsom salt by mouth: Plasma: magnesium, 4.0; calcium, 17.3. No twitching; resting quietly.

Case 17.—*Eclampsia.* I. H., a woman, aged 47, at the University Hospital, was pregnant and had frequent headaches and general muscular twitchings passing into convulsions. Plasma: Nonprotein nitrogen, 33; creatinine, 2.1; magnesium, 1.0; calcium, 11.3. After 25 Gm. of magnesium sulphate by mouth: Plasma: magnesium, 5.87; calcium, 14.13. No twitching or convulsions.

Case 18.—*Glomerulonephritis.* W. C., a man, aged 51, at the Northwestern Hospital, had violent convulsions (uremia) and a blood pressure of 160 systolic, 100 diastolic. Plasma: nonprotein nitrogen, 175; creatinine, 18; magnesium, 0.9; calcium, 24.0. No epsom salt was given.

Case 19.—*Parathyroid deficiency.* H., a man, aged 61, in the University Hospital, with a blood pressure of 130 systolic, 90 diastolic, had marked convulsions. Plasma: nonprotein nitrogen, 30; creatinine, 1.8; magnesium, 0.93; calcium, 7.0. No epsom salt was given.

Case 20.—*Possible cerebral injury.* M., a woman, aged 20, in the University Hospital, had general muscular twitching. The physical examination was negative and an encephalogram was negative. Plasma: magnesium, 1.14; calcium, 10.0. No epsom salt was given.

Case 21.—*Epilepsy (?).* McK., a boy, aged 12 years, in the University Hospital, had intermittent twitching of the upper and lower extremities every two or three days, followed by sleep for several hours (possible epilepsy). Plasma: magnesium, 1.16; calcium, 11.8. No epsom salt was given. Was relieved later by ketogenic diet.

Case 22.—*Parathyroid deficiency.* B., a woman, aged 42, in the University Hospital, had light convulsion. The laboratory report was negative. Plasma: magnesium, 1.35; calcium, 9.0. No epsom salt was given.

Case 23.—*Epilepsy.* E. E., a woman, aged 35, in the Minneapolis General Hospital, had epileptic attacks every two to three months and was restless between attacks. The laboratory report was negative. Plasma: magnesium, 1.77; calcium, 12.9. No epsom salt was given.

Case 24.—*Epilepsy.* D., a woman, aged 42, had epilepsy (grand mal, occasional attacks). The laboratory report was negative. Plasma: magnesium, 1.8; calcium, 13.7. No epsom salt was given.

It will be noted that two of these are cases of parathyroid tetany. This accords with the experimental results of McCollum and his collaborators and with the clinical observations of Howland and Marriott,[12] Denis

7. Blackfan, K. D., and Hamilton, Bengt: Boston M. & S. J. **193:** 617 (Oct.) 1925. Blackfan, K. D., and McKhann, C. F.: Acute Glomerular Nephritis in Children, J. A. M. A. **97:** 1052 (Oct. 10) 1931.

8. Dorsett, L.: Am. J. Obst. & Gynec. **11:** 227 (Feb.) 1926.

9. McNeile, L. G., and Vruwink, John: Magnesium Sulphate Intravenously, J. A. M. A. **87:** 236 (July 24) 1926.

10. Hirschfelder, A. D., and Haury, V. G.: Proc. Soc. Exper. Biol. & Med. **30:** 1157 (May) 1933.

11. Kruse, H. D.; Orent, E. R., and McCollum, E. V.: J. Biol. Chem. **96:** 519 (May) 1932, **100:** 603 (May) 1933. Orent, E. R.; Kruse, H. D., and McCollum, E. V.: Am. J. Physiol. **101:** 454 (Aug.) 1932. Kruse, H. D.; Schmidt, Marguerite M., and McCollum, E. V., ibid. **105:** 635 (Sept.) 1933.

12. Howland, John, and Marriott, W. McK.: Quart. J. Exper. Med. **11:** 289 (July) 1918.

and Talbot,[13] and Bulger and Gausmann,[14] who also found low blood magnesium in some but not in all cases of parathyroid tetany. Moreover, Salvesen and Linder[15] and Lang[16] found that removal of the parathyroid glands in animals caused no change in blood magnesium.

Three of our patients with low plasma magnesium suffered from idiopathic epilepsy. Denis and Talbot also had reported two. But since we have also found practically normal plasma magnesium in four epileptic patients (1.77, 1.97, 2.13 and 2.6 mg., respectively) it is evident that a low plasma magnesium is not a constant finding in this disease. It is possible, however, that there may be a variability in the plasma magnesium of such individuals and that periods of low magnesium may precede and accompany the attacks. We are at present engaged in a further study of this question.

Four of the patients with low plasma magnesium had glomerulonephritis. That this should occur in spite of the diminished ability of the nephritic kidney to excrete magnesium may seem paradoxical, but since such patients are usually on a milk or at least on a soft diet, it is evident that their intake of magnesium salts can easily remain below their power to excrete magnesium. When the usual purgative dose of epsom salt was administered by mouth to three of these patients, the plasma magnesium rose within from four to six hours from the previous concentrations of 0.95, 1.09 and 1.37 mg. per hundred cubic centimeters, respectively, to 3.3, 3.78 and 4.0 mg., nearly double the normal concentration; and simultaneously with this increase in magnesium the twitchings or convulsions subsided.

Denis and Talbot have reported also one case of lobar pneumonia and one case of bronchopneumonia, both of which presented convulsions, and one case of chorea with low blood magnesium. However, we have had a case of chorea with normal plasma magnesium (2.13 mg.) and normal calcium (12.2 mg.).

In view of the cases here reported, it is evident that there is a clinical syndrome associated with low plasma magnesium accompanied by a condition of hyperirritability of the neuromuscular system, often associated with muscular twitchings or convulsions. These cases are probably more common than has been realized.

At least in the patients whose kidneys are pathologic the twitchings or convulsions can be relieved by the administration of a purgative dose of epsom salt by mouth.

SUMMARY AND CONCLUSIONS

1. When normal individuals take epsom salt by mouth they excrete about 40 per cent of the ingested magnesium in the urine in twenty-four hours; but the concentration of magnesium in the blood plasma does not rise appreciably.

2. The concentration of magnesium in the plasma may vary greatly under clinical conditions.

3. There is a clinical syndrome of high plasma magnesium (hypermagnesemia) accompanied by somnolence or coma.

4. This may be induced in patients with renal insufficiency by the oral administration of one or more purgative doses of epsom salt.

5. Many cases of coma in nephritic patients, diagnosed uremic coma, may be simply magnesium coma induced by epsom salt purgation. From such coma patients could probably be awakened by intravenous calcium chloride.

6. Sodium sulphate is preferable to epsom salt for patients with renal insufficiency.

7. There is a clinical syndrome of low plasma magnesium (hypomagnesemia) accompanied by muscular twitching or by convulsions.

8. When this occurs in patients with renal insufficiency, the twitchings or convulsions are relieved by oral administration of epsom salt.

13. Denis, W., and Talbot, F. B.: Calcium in the Blood of Children, Am. J. Dis. Child. **21:** 29 (Jan.) 1921.
14. Bulger, H. A., and Gausmann, F.: J. Clin. Investigation **12:** 1135 (Nov.) 1933.
15. Salvesen, H. A., and Linder, G. C.: J. Biol. Chem. **58:** 635 (Dec.) 1923.
16. Lang, K.: Ztschr. f. klin. Med. **122:** 206, 1932.

SUDDEN DEATH FROM DINITROPHENOL POISONING

REPORT OF A CASE WITH AUTOPSY

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AND
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LOS ANGELES

In an article in July 1933, Cutting, Mehrtens and Tainter[1] stressed the remarkable potency of dinitrophenol as a metabolic stimulant and brought forward evidence (based on extensive animal experimentation and a small series of human cases) that its administration in proper dosage accelerates cellular metabolism apparently without harmful effects. They therefore proposed its carefully supervised clinical use in the treatment of "obesity, hypothyroidism, and similar depressed metabolic states." However, because of its known toxic properties they warned that "there are limitations to and possible dangers from the use of this drug clinically. It should be used only under strictly controlled conditions." This warning was emphasized in an editorial[2] and by a preliminary report of the Council on Pharmacy and Chemistry of the American Medical Association,[3] which appeared in the same issue (July 15) of THE JOURNAL. The editorial stated that "a drug with the potency and effects of dinitrophenol is a two-edged sword with appalling possibilities for harm as well as for good" and warned that "certainly for the present, at least, such investigations should be largely limited to controlled studies in hospitals by physicians competent in evaluating the effects of the drug, and with laboratory facilities capable of accurately determining blood, body tissue and other changes."

In a series of fourteen cases of obesity treated with dinitrophenol as recommended by Cutting, Mehrtens and Tainter, Anderson, Reed and Emerson[4] observed one case of what they term allergic "qualitative idiosyncrasy" with striking cutaneous manifestations. This patient had received an oral dose of 39.3 mg. per kilogram of body weight over a period of fourteen days, and the authors do not regard this as an instance of repeated small therapeutic doses producing toxic effects similar to those described for larger doses. The probability of an allergic etiology is strengthened by the early work of Mayer (reviewed by Perkins[5]). Mayer

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1. Cutting, W. C.; Mehrtens, H. G., and Tainter, M. L.: Action and Uses of Dinitrophenol, J. A. M. A. **101:** 193 (July 15) 1933.
2. Dinitrophenol, a Metabolic Stimulant, editorial, J. A. M. A. **101:** 213 (July 15) 1933.
3. Council on Pharmacy and Chemistry: Alpha-Dinitrophenol, J. A. M. A. **101:** 210 (July 15) 1933.
4. Anderson, H. H.; Reed, A. C., and Emerson, G. A.: Toxicity of Alpha-Dinitrophenol: Report of Case, J. A. M. A. **101:** 1033-1035 (Sept. 30) 1933.
5. Perkins, R. G.: A Study of Munitions Intoxications in France, Pub. Health Rep. **34:** 2335 (Oct. 24) 1919.

studied the effects of dinitrophenol on munitions workers who handled the material during the manufacture of explosives. Until hygienic preventive measures were instituted, many of these individuals developed dizziness, headache, vomiting, high fever, night sweats, and similar disturbances, and in some instances sudden death occurred. Mayer discovered that the exposed workers evinced wide variations in their susceptibility to the dinitrophenol. These variations were wholly unpredictable, except that persons with chronic rheumatism, tuberculosis, alcoholism, renal disorders and hepatic disease seemed to have a lessened resistance to the substance. Undoubtedly Cutting, Mehrtens and Tainter [5] had these experiences in mind when they commented: "Finally, the possibility of an idiosyncrasy such as an unusual sensitivity or atypical response to the drug should be kept in mind, although we have not seen unusual reactions. In view of these things, we urge that, for the present, dinitrophenol be used only as an experimental therapeutic procedure in carefully selected patients under close observation by the physician."

Further proof that dinitrophenol may possess treacherous toxic possibilities was afforded by the work of Masserman and Goldsmith.[6] They selected eighteen patients between 18 and 40 years of age, free from discoverable organic disease, whose psychobiologic underactivity was evidenced by sluggishness, passivity and apathy. These patients were given 60 mg. of sodium dinitrophenol daily and the dose was increased 60 mg. every third day to a maximum of 5 mg. per kilogram in divided doses, or until adverse symptomatology contraindicated further treatment. Six of the eighteen patients showed some improvement in their mental state. The results were indeterminate in eight cases. Toxic effects characterized by fall in blood pressure, tachycardia, acidosis and progressive stupor were observed in five cases, in one of which death occurred. These authors conclude that "dinitrophenol may possess a cumulative toxic activity which is not heralded by excessive sweating, dermatitis or pyrexia but which seems, on the other hand, to be characterized by a fall in the blood pressure, tachycardia, the onset of acidosis, and progressive torpor."

In spite of these repeated warnings it is not surprising that the use of dinitrophenol has not been restricted to the carefully controlled conditions urged by every one who has written authoritatively on the subject. Perhaps such restriction is too much to expect when an inexpensive chemical holds out promise of being a delightfully simple answer to the prayers of many men as well as of maidens. He who points a comparatively short and easy route to weight reduction will be rewarded with the rapturous gratitude of obese patients; and the patient with a passion for slimming will addict himself with pathetic fanaticism to a method which may spare him the safer but more uncomfortable procedures. It appears that within the past few months dinitrophenol has been sold and ingested, with and without prescription, in alarming quantities. We have investigated a number of drug stores in this locality, and the number of prescriptions for dinitrophenol to be seen on file at the end of a single day is disquieting. Worse than this, however, is the practice on the part of some pharmacists of selling the substance over the counter to any and every applicant, without prescription and without adequate precautions. In the case we are recording, the dinitrophenol was sold to a girl who had heard of the remedy from a friend and the label merely bore the pharmacist's instructions of how many capsules to take each day. This, we believe, is the third reported instance of death due to dinitrophenol. One case has been recorded by Masserman and Goldsmith [6] and one by Geiger.[7] Geiger's case, however, was apparently a proved result of heavy overdosage.

6. Masserman, J. H., and Goldsmith, Harry: Dinitrophenol: Its Therapeutic and Toxic Actions in Certain Types of Psychobiologic Underactivity, J. A. M. A. **102**: 523-525 (Feb. 17) 1934.

REPORT OF CASE

History.—M. B., a white woman, aged 25, single, weighing 147 pounds (66.7 Kg.) had never been seriously sick but in recent years, for pure esthetic reasons, had worried about her obesity. She was employed as a social service worker (in a county health center) and in June 1933 she consulted one of the physicians at the health center, complaining of obesity, "lack of pep" and dysmenorrhea. At this time her basal metabolic rate was found to be —12. The physician prescribed desiccated thyroid, one-fourth grain (0.016 Gm.) three times a day, and the patient continued to take thyroid tablets, probably quite constantly, until March 2, 1934. Since her work brought her into daily contact with capable physicians, it may reasonably be assumed that during this period she at no time complained of any alarming symptoms of thyroid overdosage. She lived with her parents, who assure us that she appeared to them to be in good health and good spirits.

During the afternoon of March 2, 1934, her duties took her to the office of Dr. F., with whose office nurse, Miss W., she fell into a conversation. She confided to Miss W. that she wished to reduce her weight, and that she had been taking thyroid preparations for some months with altogether inadequate effect. It happened that during lunch, that day, Miss W. had heard some doctors discussing a new reducing agent—dinitrophenol—and had herself bought some capsules of the compound from the pharmacist in a nearby drug store. Miss W. told of her discovery and later was informed by the pharmacist that the patient purchased some dinitrophenol from him on the same day (March 2). Miss W. is positive that the patient had never heard of dinitrophenol until she informed her of the substance and of the properties claimed for it. The parents are certain that their daughter ingested her first dinitrophenol capsule March 2.

The pharmacist, Mr. B., states that he sold the patient thirty-five capsules of dinitrophenol (Eastman Kodak Company's 2,4 Sodium Dinitrophenol), each capsule containing 3 grains (0.2 Gm.). The box, and what remain of the capsules, are in our possession. The label on the face of the box is imprinted with the name of the pharmacy and bears typewritten instructions "one capsule the first day, two the second, three the third, and four thereafter." The contents of the capsules are not named or described.

On Monday, March 5, the patient met Miss W. again and told her that she was taking dinitrophenol and that she "wasn't feeling so well." She attributed her feelings to the fact that the action of the thyroid had not yet "worn off" and that in some way the combined action of the dinitrophenol with the thyroid was producing uncomfortable results. However, she opined that the thyroid effect would soon disappear and did not propose curtailing her dinitrophenol program.

Tuesday, March 6, while at work, she complained of headache, backache, weakness, dizziness, shortness of breath, and excessive perspiration. Her companions assured her that the weather was to blame, and she did not leave work.

Wednesday, March 7, she felt unable to go to work but did not stay in bed, attributing her symptoms to an oncoming cold. During the day the parents noticed that she took two of the dinitrophenol capsules. About 6 p. m., she became restless and complained of the increasing severity of her headache, pains in legs and arms, and of a sensation of "burning up." She appeared flushed, perspired profusely, and this so impressed a friend who called about 8 p. m. that he anxiously volunteered to go and buy a thermometer. Instead, the parents decided to call a physician. The physician did not know that the girl had been taking dinitrophenol but her condition appeared to him

7. Geiger, J. C.: A Death from Alpha Dinitrophenol Poisoning, J. A. M. A. **101**: 1333 (Oct. 21) 1933.

so alarming that he referred her immediately to the Los Angeles County General Hospital. All this time she complained more and more bitterly of the sensation of "burning up" and kept calling for water. She vomited violently several times and became comatose about 1 a. m. while en route to the hospital in an ambulance. In removing the patient from the ambulance, the driver noticed that the sheets and cot were wet with perspiration.

The family history was not significant. The patient's childhood diseases were measles, pertussis and chickenpox. Her menses began at the age of 14 and were always somewhat irregular and attended by considerable discomfort. As already mentioned, she visited a physician in June 1933, complaining of obesity, "lack of pep" and dysmenorrhea.

Physical Examination (in hospital admitting room 3:30 a. m., March 8).—The temperature was 101.8 F., pulse 140, respirations 56. The blood pressure was not recorded. Dr. Hauser, who examined the patient, states that he is sure the temperature (recorded by a nurse) was higher than the record shows. Probably such a high respiratory rate would preclude an accurate determination of the mouth temperature. (However, in the fatality observed by Masserman and Goldsmith [6] the highest rectal temperature was 102, just before death.)

The patient was comatose and could not be aroused but was restless, perspiring profusely, and breathing deeply and rapidly. The extremities were flaccid, and no reflexes could be elicited. The pupils were regular but failed to react to light or in accommodation. The heart rate was very rapid, and auricular fibrillation was suspected.

In the admitting room a tentative diagnosis was made of polioencephalitis, and the patient was sent to the communicable disease unit, where preparations were immediately made to do a spinal puncture. However, the patient died suddenly at 4:35 a. m., before the spinal puncture could be completed. Artificial respiration, caffeine sodiobenzoate and intracardiac epinephrine were given with no response. The body came to autopsy ten hours after death, having been well preserved at optimal temperature.

Autopsy.—Livor mortis was marked over the head, neck, upper extremities and thorax. Moderate rigor mortis was present.

The pupils were equal and regular, each measuring 5 mm. in diameter. The sclerae were distinctly yellowish (causing us to suspect jaundice) and the conjunctival vessels were engorged. Fat over the sternum measured 3 cm. in thickness and over the abdomen 5 cm.

The meninges appeared normal. Coronal serial sections through the brain revealed no gross evidence of pathologic change.

The pleural surfaces were smooth and glistening and the pleural cavities contained no fluid. The right lung weighed 480 Gm. and the left 380 Gm. There was no evidence of consolidation or bronchopneumonic patching. All lobes were crepitant, but cut surfaces of the lungs at all levels appeared hyperemic, and bloody fluid exuded freely on the slightest pressure. The bronchi contained no excessive or abnormal secretion.

The heart was normal in size and shape and weighed 220 Gm. The pericardium was smooth and glistening. No endocardial lesions were present. The valve orifices were not dilated or narrowed and the valve leaflets showed no thickening. The myocardium was somewhat flabby. The coronary vessels were thin walled and patent throughout their course. The intimal surface of the aorta was pale and smooth and presented no evidence of syphilitic or atherosclerotic changes.

The esophagus was normal. The stomach contained about 300 cc. of faintly blood-tinged fluid. The gastric mucosa was intact and gave no indication of having been in contact with any irritating or corrosive material. However, there were many reddish blue areas of discoloration apparently due to small submucosal hemorrhages, and toward the cardia these areas were confluent, so as to impart to this region a uniformly bluish hue. The duodenum and upper half of the jejunum also showed some of these small hemorrhages, which probably represent the effects of much violent vomiting.

The liver was dark brown, firm, and weighed 1,400 Gm. The cut surface had a finely mottled appearance, which was by no means marked enough to suggest chronic passive congestion. The gallbladder was filled with brown bile, and the extrahepatic biliary passages were patent.

The spleen was slightly larger than normal, dark purple, quite firm, and weighed 190 Gm.

Multiple sections through the pancreas revealed no gross evidence of pathologic changes.

The kidneys were normal in size and shape and together weighed 250 Gm. The capsules stripped with ease, leaving a smooth, somewhat purplish surface. The cortex was of normal thickness. The suprarenals showed no remarkable change.

The fimbriated ends of the fallopian tubes were sealed against the ovaries by rather firm adhesions and the tubes were slightly distended and contained a small amount of turbid fluid. The ovaries and uterus appeared normal.

The urinary bladder contained 300 cc. of clear urine, which was strikingly yellow, the color being especially noticeable in the foam when the urine was agitated. The urine was aspirated before the bladder was opened and saved for examination. The bladder itself appeared normal.

Unfortunately, dinitrophenol poisoning was not suspected at the time the urine was examined, so that no chemical tests were made to determine the presence of the compound in the urine. The reaction of the urine was alkaline. The specific gravity was 1.025. Examination revealed: albumin, two plus; bile pigments, negative; sugar, acetone and diacetic acid, negative; benzidine test for occult blood, negative. Microscopic examination revealed a few granular casts.

Blood chemistry, post mortem, showed creatinine, 2.5.

Blood culture, post mortem, gave no growth after twelve days' incubation.

MICROSCOPIC EXAMINATION

Fortunately, consent for autopsy was obtained almost immediately, and in the interval the body was kept in a refrigerated cubicle. Hence there were practically no postmortem changes and it was possible to make accurate interpretations of microscopic sections.

The convoluted tubules of the kidneys showed the most striking changes. They were in all stages of degeneration. In some places there was only cloudy swelling and pyknosis, but most of the tubules showed actual necrosis. Between the tubules the interstitial tissue appeared edematous. There was much fine hematogenous pigment in the tubular epithelium, especially in the bases of the cells (fig. 1). The capillary and arterial loops in the glomeruli were distended in places. The blood vessels in the pyramids were markedly distended and there were occasional small hemorrhagic areas.

There were very extensive areas of disintegration and separation of liver cells, apparently by fluid. These areas were confined to the periphery of the lobules, the central portions being unaffected (fig. 2). As a result of these peculiar changes, each lobule appeared widely separated from the adjacent lobules. The cytoplasm of the liver cells in the periportal areas was granular and the nuclei were pyknotic (fig. 3).

The splenic pulp was unusually full of blood.

The small blood vessels of the mucosa of the stomach were markedly distended and in places actual small hemorrhages seemed to have occurred into the mucosa. The mucosa appeared very edematous, and the glandular epithelium was disintegrated and contained an abnormal number of lymphocytes.

The pancreatic tissue was unusually well preserved, and this probably constitutes good evidence that changes seen in other organs cannot be assumed to be due to postmortem changes.

There was marked congestion of the alveolar walls of the lungs. In places there was considerable edema in the alveoli.

There was marked segmentation and fragmentation of the cardiac muscle fibers in all sections (fig. 4). The tissue of the spinal cord, pons and medulla was hyperemic and the capillaries were uniformly distended with blood. There was no perivascular edema and no perivascular round cell infiltration. Section through the pons at the level of the eighth nerve showed slight ganglion cell degeneration.

CHEMICAL TESTS OF TISSUE

A measured quantity of kidney tissue was acidified and steam distilled for approximately one hour. The resulting distillate was colorless but turned canary yellow on the addition

of ammonium hydroxide. The color disappeared again when acid was added.

Since dinitrophenol is a standard indicator whose p_H range is known, the indicator properties of a solution of the distillate were compared with those of a solution of dinitrophenol diluted so as to have the same intensity of color. The color changes occurred at approximately the same p_H value.

In accordance with tests described by the French workers,[8] 200 Gm. of liver tissue was immersed in 95 per cent alcohol for five days, and the resulting extract displayed the same indicator properties as the kidney distillate.

Both the solutions thus obtained from kidney and liver gave a positive Le Mithouard reaction. This test and many others are described in detail by Magne, Mayer and Plantefol.[8]

Finally, 400 cc. of the kidney extract was concentrated by evaporation to 10 cc. This concentrate gave a strongly positive reaction when tested according to the method of Derrien. The technic of the reaction of Derrien is quoted from the French workers by Anderson, Reed and Emerson.[4]

COMMENT

Following the autopsy we were unable to propose so much as an intelligent guess regarding the cause of death; therefore the patient's relatives were questioned regarding the possibility of her having ingested mushrooms (several deaths from mushroom poisoning having been reported in this district recently) and regarding any medicine she might have been taking. The mushroom theory was ruled out, but the father did recall seeing her take some "pink capsules" and these he brought to us the next day. The capsules contained a yellow crystalline powder and this immediately called to our minds the peculiar yellowness of the urine, which, unfortunately, we had by this time discarded. A young obese woman might have been trying to reduce her weight and might have been using dinitrophenol. We compared the substance in the capsules with a sample of dinitrophenol and they appeared identical. The melting point was found to be 114 F. The substance was readily soluble in water, and the solution became colorless on the addition of acid and yellow again when alkalinity was restored. Later we talked with the pharmacist from whose store the purchase was made. He confirmed our presumption that the capsules contained dinitrophenol and referred us to Miss W., a friend of the deceased. From these persons and from the family we were able to piece together and substantiate the history as related.

In the box brought to us by the father were nineteen capsules of dinitrophenol. Since thirty-five capsules were sold to the deceased, she obviously took sixteen capsules between March 2 and March 7 inclusive. This harmonizes exactly with the instructions on the label to take "one capsule the first day (March 2), two the second, three the third, and four thereafter." It may reasonably be assumed that she took one on Friday (March 2), two on Saturday, three on Sunday, four on Monday, four on Tuesday, two Wednesday morning and none Wednesday afternoon, when her symptoms became more prominent. Each capsule contained 180 mg. of dinitrophenol, so that a total dose of 2,880 mg. was taken in a period of five days.

It seems to us indisputable that this girl's sudden death is attributable directly to the action of dinitrophenol.

THERAPEUTIC DOSAGE OF DINITROPHENOL

Cutting, Mehrtens and Tainter[1] gave nine patients daily oral doses of from 3 to 5 mg. per kilogram of body weight, with no ill effects. In their series of fourteen cases, Anderson, Reed and Emerson[4] gave fourteen patients daily oral doses of about 3 mg. per kilogram, with one case of sublethal toxicity. Apparently a daily oral dose of from 3 to 5 mg. per kilogram is the accepted safe therapeutic dosage.

This figure was based largely on animal experimentation. Tainter and Cutting[9] found that the average fatal dose for 50 per cent mortality in rats, dogs and rabbits was between 20 and 30 mg. per kilogram. Magne, Mayer and Plantefol[8] concluded from studies of a large and varied series of animals that the reliably fatal dose was about 50 mg. per kilogram. To human subjects, Mehrtens and Tainter[1] have given as high as 10 mg. per kilogram for a small number of doses.

When our patient took four capsules a day (or 10.7 mg. per kilogram daily) she was consuming more than the recommended therapeutic dose but was well below the limit of what is thought to be the fatal dosage.

IDIOSYNCRASY TO DINITROPHENOL

From the evidence available it seems probable that, as compared with animals, human beings have a more variable and more unpredictable susceptibility to dinitrophenol. Magne, Mayer and Plantefol[8] found that only a small number of animals succumbed to a dose smaller than the generally effective lethal dose for their particular kind. Tainter and Cutting[9] also observed that the limit of tolerance was fairly regular within each animal species, though some species, particularly the pigeon, succumbed to a dose which other animals could tolerate with safety. While certain responses, such as the fever, were very variable, in no single instance, apparently, did an experimental animal die unexpectedly as a result of a dose of dinitrophenol which for other animals of the same species was demonstrably well below the safety limit.

This relative uniformity of tolerance is apparently not true of the human subject, and if not true it is the point to be stressed. Naturally there is no large well controlled series of human cases on which a conclusion might be based. But we have already pointed out that Mayer[5] discovered a striking variation in the susceptibility of the men and women who handled dinitrophenol in the French munitions factories during the war. A group of people doing the same type of work in identical surroundings often manifested responses varying apparently all the way from a complete absence of deleterious symptoms to sudden death. The preliminary report of the Council on Pharmacy and Chemistry[2] points out that "these accidents grew so numerous that it was proposed at one time to abandon the manufacture of this compound despite the then great demand for it."

Aside from the small series of cases reported by Cutting, Mehrtens and Tainter,[1] the only carefully controlled clinical trials of dinitrophenol have been conducted by Anderson, Reed and Emerson,[4] who encountered one case of serious toxicity in a series of fourteen, and by Masserman and Goldsmith,[6] who observed four cases of toxicity and one death in a series of eighteen. Perhaps the increasingly widespread and promiscuous use of the compound will have at least one good result. It may provide in an unpleasant manner evidence of the human responses to dinitrophenol. The case we are recording is the third fatal example of this probability.

8. Magne, H.; Mayer, A., and Plantefol, L.: Ann. de physiol. and physiochem. biol. **8**: 1-176, 1932.

9. Tainter, M. L., and Cutting, W. C.: Miscellaneous Actions of Dinitrophenol, J. Pharmacol & Exper. Therap. **49**: 187-208 (Oct.) 1933.

The total dosage in this case (weight 67 Kg.) was 2.88 Gm. in five days. In the case recorded by Anderson, Reed and Emerson [4] (weight 79 Kg.) the total dose was 3.15 Gm. over a period of fourteen days. In both instances the total amount of dinitrophenol consumed was well within the estimated safety limits, and the victims probably each had an abnormal susceptibility

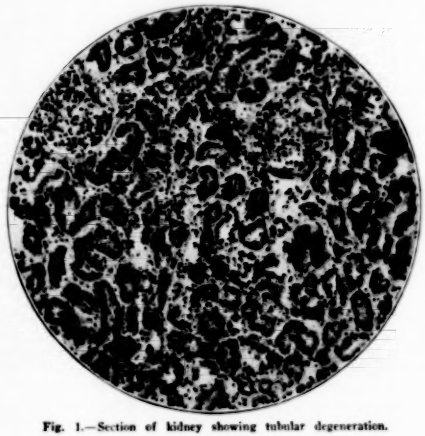

Fig. 1.—Section of kidney showing tubular degeneration.

to dinitrophenol. The outstanding difference is that our patient had been taking thyroid for several months before she began to use dinitrophenol. There is a possibility, on which we are not competent to pass judgment, that the fatality was due to some vicious synergism between the action of dinitrophenol and of thyroid. It is more probable that our case represents, like that reported by Anderson, Reed and Emerson,[4] an allergic idiosyncrasy to dinitrophenol.

The patient observed by Masserman and Goldsmith [6] received 6.06 Gm. in fourteen days; but since she weighed 130 Kg. the dosage is not significantly greater, and she probably did not die of simple overdosage.

ACTION OF DINITROPHENOL

The work of Magne, Mayer and Plantefol [8] is in agreement with that of Tainter and Cutting [9] that in animals and men fever occurs from dinitrophenol administration as a result of increased tissue metabolism, apparently by a direct peripheral action on body cells. Carbohydrate seems to be singled out as the main fuel for this metabolic increase. Magne, Mayer and Plantefol showed that the rise in temperature is not due to action on the heat center, because they were able to produce it in poikilothermic animals, in anesthetized animals, in curared animals, in animals with the cord severed, and in isolated strips of muscle. Their final conclusion was that "dinitrophenol 1-2-4 seems to be a direct excitant of cellular oxidation."

Since cyanide inhibits cellular oxidation and dinitrophenol augments it, Tainter and Cutting [9] injected cyanide into pigeons at the height of their response to an injection of dinitrophenol. Methylene blue (methylthionine chloride) can be shown successfully to antagonize a similar dose of cyanide, but the pigeons protected with dinitrophenol died within one minute. Hence while dinitrophenol seems beyond doubt to act by accelerating cellular oxidation, it cannot be shown to antagonize agents that depress cellular oxidation.

CLINICAL SIGNS AND SYMPTOMS

Probably one of the most treacherous properties of dinitrophenol is that it seems to induce a relative euphoria in subtoxic doses. Thus Cutting, Mehrtens and Tainter [1] observed that their nine patients treated for obesity "did not suffer from any deleterious symptoms, as a result of their reducing treatment. On the contrary, they felt better and more active than before." We suggest that this may be a treacherous property, because it seems to us that it may betray the patient into a false sense of well being. From our present understanding of the subject it is clear that the responses of a few patients cannot safely be used as a criteria for other individuals. For the present the only safety lies in confining the clinical use of the drug to very closely supervised cases.

Hyperthermia with profuse perspiration and what the French call "thermic dyspnea" seem to be the outstanding signs of toxicity. Cutting, Mehrtens and Tainter [1] found that, in a series of eight patients, single doses between 5 and 10 mg. per kilogram provoked no changes in temperature, pulse or respiration but did cause copious sweating. Three single doses "of more than 10 mg. per kilogram gave increases in temperature of 3 degrees C. or more, in respiration of 15 to 30 per minute, and of pulse 20 to 30 per minute. . . . The latter doses are considered too dangerous for routine use." Probably it is wise to stress this warning. The first sign of abnormal sweating or elevation of temperature (or

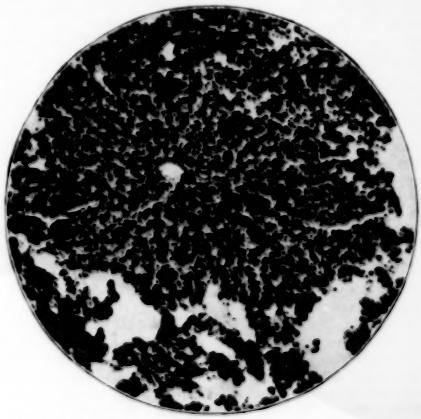

Fig. 2.—Section of liver, under low power, showing peculiar separation of liver cells in the periphery of the lobule.

according to Masserman and Goldsmith [6] fall in blood pressure and tachycardia) should call for abrupt discontinuance of the medication, for, as Cutting, Mehrtens and Tainter [1] state, the "margin between the febrile and the fatal dose is narrow."

Various tests have been devised, especially by the French workers, for the detection of dinitrophenol in blood, urine and certain viscera. Their importance, for

the present, seems to lie mainly in helping to establish cause of death in a disputed case. According to Perkins, a persistence or increase in amount of dinitrophenol in the urine (measured by the Derrien test) should be considered a sign of intolerance. In our case it seems probable that Derrien's test would have been positive, since the urine was strikingly yellow. However, in the case recorded by Anderson, Reed and Emerson, Derrien's test was repeatedly negative, so that it cannot be regarded as a means of testing allergic sensitivity to the compound.

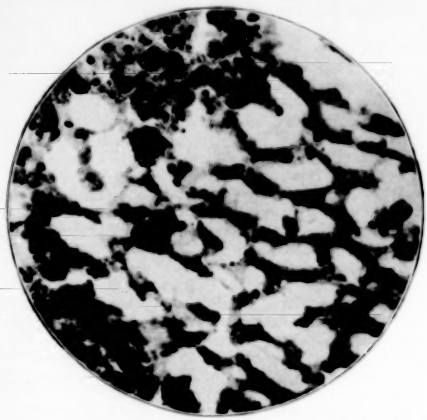

Fig. 3.—Section of liver, under high power, showing degeneration of liver cells in the periphery of the lobule.

TREATMENT OF DINITROPHENOL POISONING

Tainter and Cutting [9] injected six rabbits with from 20 to 40 mg. of dinitrophenol, and when the usual respiratory and temperature changes developed, the rabbits were given from 10 to 40 mg. of morphine. The rise in temperature was checked and the respiratory rate returned to normal, but all the animals died. Other depressants, such as barbital and chloralose, were equally disappointing. These facts indicate that while morphine may be useful to counteract excitement and dyspnea (and is so recommended by Perkins [8]) it cannot be regarded as a true antidote and will not save life in a case of severe poisoning.

Tainter and Cutting [9] then tried agents calculated to reduce muscular or cellular activity and to reduce local blood flow. All these agents, such as sodium gluconate, dextrose plus insulin, monoiodoacetic acid, quinine and salicylate, were found ineffective in animals.

Whenever dinitrophenol is used clinically it should therefore be borne in mind that there is no known antidote and that, once the process of intoxication begins, no means of arresting it are available. The action of the agent cannot be opposed. At present one can merely try to support the organism through the crisis. Mayer [5] found (in treating munitions workers) that this could best be done by giving massive intravenous injections of dextrose. In animals, Tainter and Cutting [9] found that the only measures which affected the mortality were administration of fluids, and cooling baths.

PATHOLOGY OF DINITROPHENOL POISONING

Hundreds of experimental animals have been examined post mortem but no lesions peculiar to dinitrophenol poisoning have been described. Mayer [5] in 1915 was the first physician who had the opportunity of studying tissues of human victims. He found that, while edema of the lungs and fatty infiltration of the liver may occur, there are no characteristic lesions.

Our case probably presents the first microscopic study of tissue taken at autopsy since Mayer's early work, and we have added very little. Even if the lesions we observed were unique, it would be rash to consider them pathognomonic on the strength of one case. However, the lesions in the kidney, liver and heart seem to us sufficiently arresting to warrant careful description. The pronounced tubular degeneration has been understressed and may signify that dinitrophenol acts on the kidney in a manner similar to other poisons, such as corrosive mercuric chloride and phosphorus. The peripheral spacing and early degeneration of liver cells seems to us a most unusual finding and is well seen in the photomicrograph. Fragmentation of the cardiac muscle fibers probably indicates the severity of the intoxication and a sudden, agonizing death.

CONCLUSIONS

1. Every one who has commented on the use of dinitrophenol has stressed the importance of restricting its clinical trials to carefully selected cases under constant supervision. However, it appears that the compound is being widely popularized as a weight-reducing agent and is being bought and used with no competent direction. This seems highly deplorable in the present state of knowledge of human responses to dinitrophenol.

Fig. 4.—Fragmentation and segmentation of heart muscle fibers.

2. Thorough and extensive animal experiments have been performed (notably by Tainter and Cutting [9] and by Magne, Mayer and Plantefol [6]) and the toxic effects and the fatal dosage for animals have been accurately determined. This work, however, must not be presumed on too freely in dealing with human beings, and it can have no value whatever in predicting or preventing the occurrence of severe allergic manifestations.

3. There is no antidote for dinitrophenol poisoning. The only measures that have seemed to reduce the mortality in animals have been administration of fluids, and cooling baths. In dinitrophenol-poisoned munitions workers, Mayer found that intravenous injections of dextrose constituted the most effective treatment. This seems rational because of the marked loss of tissue glycogen that has been shown to occur. Morphine allays the excitement and the dyspnea and may check the rise in temperature, but it cannot halt the intoxicative process, and, in dogs poisoned with dinitrophenol, morphine does not affect the mortality.

4. In the case of sudden death from dinitrophenol poisoning reported, the victim heard of the compound from a friend and bought and used it without competent supervision. A physician was not consulted until a few hours before death.

5. The dosage in this case was high but within the presumed limits of safety, so the fatality should probably be regarded as an example of allergic idiosyncrasy.

6. Before taking dinitrophenol, the patient had been taking desiccated thyroid extract, one-fourth grain (0.016 Gm.) three times a day for about one year. We do not know whether or how this has significance.

A CASE OF FATAL DINITROPHENOL POISONING

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In a short note recently published,[1] attention was drawn to a fatality that occurred from dinitrophenol poisoning. Since this drug is being widely used as a metabolic stimulant, and since the complete details of this case were available only to us, it seemed desirable to publish a full account of it, together with the pathologic observations. This case report will also emphasize the fact which we have consistently stressed;[2] namely, that careless or reckless use of this drug may have unfortunate consequences.

REPORT OF CASE

History.—H. G., a man, aged 37, a graduate of a Vienna medical school but unlicensed to practice in this country, called on one of us (T.) to obtain information regarding dinitrophenol as a metabolic stimulant. He stated that he was suffering from general glandular dysfunction, including a hypopituitarism resulting from a previous sphenoiditis. His libido was gone and no therapy had been beneficial. On questioning, he admitted that the metabolic rate was normal and that he had little, if any, need of weight reduction, since he was not obese. The patient's account of his glandular dysfunction was neither tangible nor convincing. In addition, there was noticeable slurring of speech and eccentricities of manner, which aroused suspicion of some more definite disease process. He was therefore advised that the drug offered no prospect of benefit to him, since he needed neither to increase his metabolism nor to lose weight. In the resulting discussion, the pharmacologic actions of the drug and its power to produce severe or fatal hyperpyrexia were explained and apparently understood.

About a month later, one of us (T.) was asked for advice on the treatment of this man, who was in the Central Emergency Hospital, with Dr. Charles Benninger in charge, from the effects of a dose of dinitrophenol taken that day. He died, however, before the suggested cold bath and oxygen therapy could be started.

On admission to the hospital at 5:30 p. m., he told the attendants that one week previously he had taken a single 5 grain dose of dinitrophenol by mouth and that he had suffered a terrific fever for about half a day, with a loss of weight of 6 pounds (2.737 Gm.). Wishing to repeat the treatment, he said he took another 5 grain dose by mouth at 11 a. m. on the day of admission. At 5 p. m. he was taken to the Emergency Hospital suffering from hyperpnea and pain in the chest. At 7 o'clock the rectal temperature was 105.0 F., and at 9:30 105.7 F. The blood pressure was 140 systolic and 124 (?) diastolic, with a rapid pulse up to 146 per minute. Respiration was extremely rapid and deep. Treatment by the hospital staff consisted of two doses of morphine, one-fourth grain (0.016 Gm.), for the chest pain and acetylsalicylic acid, 20 grains (1.3 Gm.), for the fever. There was some restlessness and mental confusion beginning about 9 p. m., and death occurred at 10 o'clock. Twenty minutes later the rectal temperature was above the limits of the clinical thermometer (probably around 115 F.), rigor was present, and the skin appeared darkly cyanotic.

Examination of the patient's belongings by the authorities showed a box of sodium dinitrophenol capsules, of 100 mg. each, with only ten of the original hundred capsules left. Since he took the drug only twice, he must have taken ninety capsules, or 9 Gm. of the drug, in these two doses, or at least 4.5 Gm. in the final dose, which proved fatal.

Subsequent investigation revealed that he was receiving tryparsamide injections from another physician, which he had requested for syphilis of the central nervous system. The blood Wassermann reaction was negative, but he had insisted on being given the antisyphilitic therapy that would not permit a spinal fluid examination. He had also been interested in the possible use of fever therapy, such as by malaria or diathermy, in the treatment of the supposed syphilis.

From the evidence available, we cannot be sure whether he took 5 Gm. by mistake for 5 grains, as might be inferred from his statement about dosage, or whether he took a large dose deliberately, for the therapeutic effect of the high fever he knew it would produce. The latter seems the more probable explanation, since, in a conversation with a physician during the week after his first dose, he described his first experience with it as being accompanied by a very high fever, which was very beneficial. On being urged by the physician not to be so reckless again, he retorted that he would take another dose the next Sunday and that, if it resulted fatally, he would be just another martyr to science.

Necropsy.—This was performed at the San Francisco coroner's office eleven and a half hours after death. We are indebted to Dr. Sherman Leland, autopsy surgeon at the coroner's office, for permission to witness the autopsy and for the tissues given to us for microscopic study.

The body was that of a well developed, well nourished man of medium stature who appeared to be about 50 years of age. Mixed grayish brown hair was present over the scalp. The skin was of fine texture throughout and showed a barely perceptible yellowish tint. The subicteric tint was most apparent in the sclerae and conjunctivae. A marked postmortem lividity of the dependent parts was present.

The thorax and abdomen were covered by a moderate layer of yellow subcutaneous fat measuring 3 cm. in thickness. The abdominal and thoracic muscles were of normal color and appearance. The peritoneum was smooth, moist and glistening. A moderate amount of fat was contained in the long, apron-like omentum. The stomach was moderately distended, extending 2 inches below the left costal margin. Considerable gas and semisolid fecal material were retained in the colon.

A number of fibrous adhesions were scattered throughout the left pleural cavity. Both pleural cavities were free of fluid.

A large amount of fat was present in the anterior mediastinum. The pericardial sac contained a few cubic centimeters

From the Departments of Pharmacology and of Pathology, Stanford University School of Medicine.

1. Geiger, J. C.: A Death from Alpha-Dinitrophenol Poisoning, J. A. M. A. **101**: 1333 (Oct. 21) 1933.

2. Cutting, W. C.; Mehrtens, H. G., and Tainter, M. L.: Actions and Uses of Dinitrophenol, J. A. M. A. **101**: 193 (July 15) 1933. Tainter, M. L.; Stockton, A. B., and Cutting, W. C.: Use of Dinitrophenol in Obesity and Related Conditions, ibid. **101**: 1472 (Nov. 4) 1933.

of clear, straw-colored fluid. A few small ecchymotic hemorrhages were present in both visceral and parietal layers of the pericardium.

The heart was of normal size. A moderate amount of subepicardial fat was present over the right ventricle. The heart valves and chambers were normal. The heart muscle was a medium reddish brown, firm and rather moist. The endocardium was glistening and showed a moderate edema. Occasional small hemorrhagic spots were also present in the endocardium. The base of the aorta was essentially normal.

The left lung was about normal size and heavy, and on cut section it showed a marked congestion and a moderate pulmonary edema. The surface was a purplish red. The bronchi were congested and contained a small amount of bloody mucus. No frothy fluid, however, was present in the trachea or large bronchi. The peribronchial lymph nodes were small and anthracotic.

The right lung showed an old apical scar. Otherwise the lung was essentially the same as the left.

The spleen was of normal size. A few fibrous adhesions were present over the convexity. The cut section showed a dark congested pulp of firm consistency.

The left and right kidneys were of normal size, showing slight remnants of fetal lobulation. The capsules stripped readily. The surfaces were smooth and of a medium reddish brown. On cut section the parenchyma appeared normal. The peripelvic fat was moderately increased in amount. The mucosa of the renal pelves was smooth, pale and glistening.

The liver was of normal size. The capsule was smooth, except for a few tiny areas in which it appeared slightly "loose." Cut section showed a moderate degree of congestion and a slight but definite icteric tint. The liver cut with normal resistance.

Pale golden yellow bile of normal viscidity was contained in the gallbladder. The latter was of normal size. Considerable fluid of a pale yellow was present in the stomach. The color

Fig. 1.—Moderate congestion and slight detachment of liver cells. Slightly reduced from a photomicrograph with a magnification of 80 diameters.

appeared to be due to bile staining and was not the typical color of dinitrophenol.

The calvarium was of normal thickness and markings. The brain showed a definite but slight edema. A few tiny hemorrhagic spots were present in the pia over the temporal and parietal lobes.

The anatomic diagnosis was: dinitrophenol poisoning, fatal; ecchymoses of the endocardium, pericardium and pia; pulmonary edema; tuberculosis, pulmonary and apical, healed; and pleuritic adhesions.

Histologic examination of the liver showed a slight detachment of the hepatic cells from one another (figs. 1 and 2) with no apparent change in the reticulo-endothelial cells. A slight fatty infiltration was present in the periphery of the lobules.

An extreme congestion of the lung was present throughout. The septums and the alveolar walls showed a marked congestion and a slight edema. Small amounts of plasma with a few red blood corpuscles were present in some of the alveoli

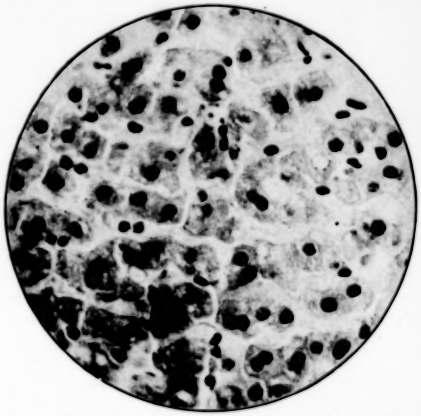

Fig. 2.—Detail of detachment of hepatic cells. Slightly reduced from a photomicrograph with a magnification of 450 diameters.

(fig. 3). In a few sections, some of the small blood vessels were filled with masses of agglutinated red blood corpuscles.

Sections of the heart showed considerable transverse fragmentation of the muscle fibers and a slight variation in the intensity of staining.

Histologically, the kidney showed a moderate congestion of both cortical and medullary portions in some areas. The glomeruli were essentially normal, aside from congestion. In scattered areas, some of the convoluted tubules showed a slight to marked cloudy swelling of the lining epithelium with beginning detachment of the lining cells.

The brain sections showed no evident abnormalities and no evidence of syphilis.

Aside from a moderate congestion of the pulp, the spleen was essentially normal.

Estimation of Dinitrophenol in the Blood.—The blood was partly hemolyzed so that a clear plasma could not be obtained. With the use of blood to which dinitrophenol had been added as a standard for comparison the content of dinitrophenol was estimated colorimetrically, by two different methods, as follows:

First method: Blood was diluted ten times with distilled water; a protein-free filtrate was obtained with sodium tungstate and sulphuric acid. Clear colorless filtrate was alkalinized with sodium carbonate and the color estimated against the standards made at the same time in normal blood. Five cubic centimeters of the patient's blood was found to contain 0.15 mg. of dinitrophenol. For a total blood volume of 10 per cent of his estimated body weight of 80 Kg., this would give 240 mg. in the blood. Or, if evenly distributed between blood and tissues, it would indicate about 2.4 Gm. of dinitrophenol in the entire body.

Second method: A 10 per cent solution of the patient's blood in distilled water and standard solutions of dinitrophenol in blood were acidified and extracted with chloroform; the chloroform was removed and the residue evaporated to dryness over a water bath. The residue was taken up in water with sodium carbonate, reacidified and extracted with chloroform.

The chloroform was evaporated off again, and the residue redissolved with sodium carbonate and distilled water up to volume. With the use of Walpole's double tube technic, against control tubes treated similarly, 5 cc. of the patient's blood was found to contain 0.19 mg. of dinitrophenol. This would give, calculated as before, 304 mg. in the blood, or 3.04 Gm. of dinitrophenol in the whole body. The average of these two results would be 2.72 Gm. of the acid dinitrophenol, or 3.31 Gm. of the sodium salt which he actually took.

We know from experiments now under way that dinitrophenol is rapidly excreted in the urine, the greater part leaving the body within twenty-four hours. Since the patient survived the administration eleven hours, during which time excretion was doubtless going on, the amounts of dinitrophenol demonstrated in the blood are in general agreement with the aforementioned conclusion; namely, that about 5 Gm. was the dose actually taken. Since the average daily clinical dose is 300 mg. of sodium dinitrophenol, he took what was probably about seventeen times the usual therapeutic dose and about eight times the highest dose we have ever given to the most resistant patients.

SUMMARY

1. A case is reported of death occurring eleven hours following the oral administration of between eight and seventeen times the usual therapeutic dose of dinitrophenol.

2. The dosage taken was estimated, by various methods, to have been at least 2.4 but more probably 5 Gm. The man weighed approximately 80 Kg., giving an estimated dosage of 62.5 mg. of dinitrophenol per kilogram of body weight.

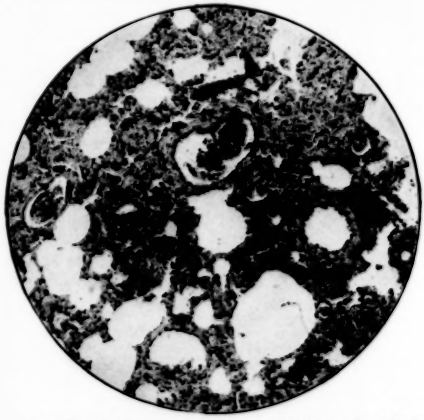

Fig. 3.—Marked congestion of alveolar and septal blood cells. Slightly reduced from a photomicrograph with a magnification of 80 diameters.

3. The drug was self administered with the apparent attempt to produce hyperpyrexia as a therapeutic measure for a supposed syphilis of the central nervous system.

4. The rectal temperature shortly after death was so high that it could not be recorded by a clinical thermometer, probably being at least 115 F.

5. The onset of rigor mortis was rapid, the body being rigid within ten minutes.

6. A subicteric discoloration of the sclerae and conjunctivae was present and was due in all probability to the color of the drug itself.

7. The anatomic changes consisted chiefly in a marked rigor mortis; an acute pulmonary congestion and edema; ecchymotic hemorrhages in the endocardium, pericardium and pia; mild nephrotic changes in the kidneys, and a slight detachment of the liver cells from one another.

8. The clinical and anatomic changes bear a striking resemblance to those seen in cases of heat stroke.

Sacramento and Webster streets.

Clinical Notes, Suggestions and New Instruments

TRANSDUODENAL DECOMPRESSION AND REINTRODUCTION BY PROCTOCLYSIS OF GASTRO-INTESTINAL DRAINAGE IN ACUTE MECHANICAL ILEUS

CARL G. ROBERTS, M.D., Chicago

Mrs. F. B., aged 45, married and the mother of two children, admitted to St. Elizabeth Hospital, July 23, 1933, had three days previously had a sudden onset of colicky pain in the epigastrium, which localized in the right lower quadrant within twenty-four hours. Simultaneously with the onset of pain she vomited repeatedly and felt as if she had a fever. After three days of ineffectual self medication, a physician was called, who advised immediate removal to the hospital.

Her previous history was essentially negative with the exception of an attack of scarlet fever in infancy and a fracture of the right seventh rib due to an automobile accident in January 1933. The family history revealed that one sister had died of pulmonary tuberculosis.

On admission her temperature was 100 F., pulse 104 and respiration rate 28. There was marked rigidity of the right abdominal muscles with pronounced tenderness at McBurney's point. The leukocytes numbered 16,800, with 90 per cent polymorphonuclears, 5 per cent lymphocytes and 5 per cent large mononuclears. The urine contained a trace of albumin, many hyaline casts, a number of epithelial cells and a few pus cells.

The general appearance of the patient was indicative of a condition more serious than was suggested by her pulse and temperature. A tentative diagnosis was made of acute appendicitis with probable rupture.

Examination through a McBurney incision disclosed a perforated gangrenous appendix, very black throughout its length, surrounded by about 180 cc. of greenish yellow, foul smelling pus. The adjacent cecal wall was edematous, discolored and congested. The appendix was removed, the pus was evacuated, and Penrose drains were placed in the paracolic fossa and pelvic basin. The muscle, fascia and skin were left unsutured, the entire operation consuming twenty-five minutes.

The pathologic examination, by Ernst Pribram, July 25, revealed that the appendix was 3 inches (7.6 cm.) long and about one-half inch (1.25 cm.) wide; the wall was thick and green throughout. The mucous membrane was necrotic. The periappendiceal tissue, 1½ inches (3.75 cm.) in diameter, was intensely infiltrated and inflamed. Microscopic examination revealed gangrenous appendicitis and perityphilitis. A smear from the abdominal wall showed pus cells yielding gram-positive and gram-negative bacteria and diplococci.

After the first two days the patient's pulse rate varied from 88 to 100, but she continued to have a septic temperature. Drainage was profuse, both smear and culture showing many gram-positive and gram-negative diplococci and bacteria.

August 3, she had a severe chill lasting twenty-five minutes, followed by a temperature of 102 F. and a pulse rate of 138. During the next twenty-four hours she was unable to void urine, and repeated catherization was necessary. August 7,

bimanual examination revealed bulging of the culdesac, and through a posterior colpotomy 500 cc. of pus was evacuated. Following this, the temperature was distinctly lower for two days, when it again became irregularly septic. Voluntary micturition reappeared after the operation, accompanied by diarrhea, which continued for a few days.

August 11, a roentgenogram revealed marked elevation of the right diaphragm with a limitation of movement, and, although no fluid level was apparent, this finding together with the persistent septic temperature was suggestive of subphrenic abscess. August 12, she was again removed to the operating room; the ninth rib was resected in the midaxillary line and the subphrenic space was entered by the transpleural route, where an abscess was found and drained.

The temperature and pulse rate gradually returned to normal, so that by August 21 they were 98.8 F. and 80, respectively. The general condition of the patient, however, was not entirely satisfactory, as the primary abdominal wound showed little tendency to heal, still draining very profusely. September 13, a blood transfusion was given to combat the severe sepsis and anemia, following which her condition improved, drainage decreased and both wounds began to heal.

October 11, she complained of cramplike pains and vomited a number of times. An enema resulted in the evacuation of a corresponding decrease in nonprotein nitrogen and carbon dioxide combining power, the pulse rate returned to normal, and on October 16 a glycerin enema resulted in the expulsion of much flatus and a large stool. The patient was given increasing quantities of liquids, and on October 22 she was able to sit out of bed.

Because of her previous operation and prolonged drainage, it was felt that the obstruction was due to adhesions involving only a part of the circumference of the intestinal wall; therefore the chances were good for spontaneous recovery of peristaltic function if distention was relieved and the inorganic salts were replaced. This conjecture proved correct; the convalescence was uneventful, no secondary operation was necessary, and the patient was dismissed, November 5.

REINTRODUCTION OF GASTRIC CONTENTS

After reading the case report of Block[1] of Philadelphia, who reintroduced the gastric contents by rectum in a case of acute dilatation of the stomach, I felt that this might be a desirable method of replacing the lost gastric and intestinal fluids in certain cases of obstructed ileus.

In the case reported by Block,[1] the use of the acid gastric secretion resulted in irritation and diarrhea, but the results otherwise were gratifying. In the duodenal contents, however,

Fig. 1.—Elevation of right diaphragm, indicating presence of subphrenic abscess, Aug. 11, 1933.

Fig. 2.—Appearance, Oct. 11, 1933, showing Levine tube in duodenum, and distended gas-filled loops of ileum arranged in vertical instead of transverse ladder formation.

Fig. 3.—Barium enema showing point of obstruction near ileocecal valve. End of tube is seen below transverse colon.

formed stool but no flatus. Nausea and vomiting increased, however, not even water being retained. On examination there was slight abdominal distention, borborygmi, visible peristaltic waves, and tenderness in the umbilical and hypogastric regions. A working diagnosis of acute ileus was made, following which a flat roentgenogram revealed gas-filled loops of ileum and a barium enema disclosed a point of obstruction proximal to the ileocecal valve.

Although the diagnosis was made within twenty-four hours of the onset, the patient's condition was so grave that it was deemed unwise to attempt even an enterostomy. The stomach was lavaged and a Levine tube passed intranasally through the stomach into the second portion of the duodenum. It was felt that, in the absence of segmentation of the bowel and a generalizing peritonitis, this would result in decompression, just as an enterostomy relieves distention. There was no further vomiting following the passing of this tube, which remained in situ for three days. The drainage material, composed of gastric, biliary, pancreatic and jejunal fluids, was collected from the tube and given to the patient by proctoclysis in quantities of 180 cc. every four hours. Hartmann's solution and dextrose were used intravenously, together with one ampoule of pitressin every three hours.

There was immediate improvement in the general condition of the patient; within forty-eight hours the pain and distention disappeared, there was an increase in blood chlorides with a the acid gastric juice is neutralized by biliary and pancreatic secretions, so that the collected fluids are alkaline in reaction and are not irritating to the normal rectal mucosa.

What of the danger from toxicity of this material? According to Elman,[2] a liter of normal intestinal contents containing trypsin, peptones, phenols, amines and other substances together with gas bacilli may be reintroduced in the normal gastrointestinal tract without any harmful results. A few cubic centimeters of some normal intestinal contents are sufficient to kill when injected in the circulation. The toxin present in intestinal obstruction does not seem to be harmful in the presence of undamaged mucosa, retaining its normal power of selective absorption;[3] therefore when reintroduced by proctoclysis not only is the drainage material harmless but its composition is probably superior and more adaptable than any synthetic solution that can be devised. The experience of Wilkie[4] is strongly corroborative of this statement.

The question of the absorptive ability of the rectum may be raised, but, in the presence of depletion of body fluid or dehy-

1. Block, F. B.: Acute Intestinal Obstruction, S. Clin. North America **12**: 1483 (Dec.) 1932.

2. Elman, Robert: Treatment of Late Acute Intestinal Obstruction, Surg., Gynec. & Obst. **56**: 175-181 (Feb.) 1933.

3. Dragstedt, L. R.; Moorehead, J. J., and Burcky, F. W.: Intestinal Obstruction, J. Exper. Med. **25**: 421-439 (March) 1917.

4. Wilkie, D. P. D.: Some Principles in Abdominal Surgery, Brit. J. Surg. **11**: 586 (Jan.) 1924.

dration with its consequent increase of blood concentration and viscosity, absorptive capacity is increased. Perusse [5] demonstrated that isotonicity is not the ideal concentration for proctoclysters, as a hypotonic solution is more readily absorbed. Dehydration secondary to the vomiting of ileus increases the blood concentration; consequently a solution even more concentrated than the gastro-intestinal fluids will be readily absorbed if given by proctoclysis.

This case is reported with the full realization that nothing can be more misleading than to base positive opinion on one or more cases without extensive scientific observation checked by proper controls. Further investigation should be based on scientific experimental research, amplified by clinical application over a considerable period of time, before logical conclusions can be reached. The results obtained in this one case were so dramatic and positive that the report seems warranted as a clinical experience, which may be an inspiration for detailed investigation and experimental research to test its merit.

152 West Division Street.

THE LINGUAL TONSILS AND SOME OF THEIR COMMON ABNORMALITIES

LESTER HOLLANDER, M.D., PITTSBURGH

Maximow,[1] in his textbook on histology, gives a clear-cut description and three excellent illustrations of the lingual tonsils. He says: "The bulgings on the root of the tongue are caused by spherical accumulations of lymphoid tissue; they are peripheral nodules with germinal centers—the lingual tonsils and the follicles of the tongue. On the free surface of each of them a small opening can be noticed. It leads into a deep, irregular invagination lined with stratified squamous epithelium—the crypt. The epithelium of the crypt is surrounded by lymphoid tissue; innumerable lymphocytes infiltrate the epithelium and assemble in the lumen of the crypt, where they degenerate and form masses of detritus with desquamated epithelial cells and bacteria. The excretory ducts of the follicles open into the crypt or on the free surface."

The importance of the lingual tonsils arises from the fact that a considerable number of the medical profession is not mindful of their existence and also that some of the abnormalities which occur in them are not sufficiently familiar. Although they may be involved in any one of what Boyd [2] calls the "big four" of pathologic changes of the tongue—syphilis, carcinoma, tuberculosis and inflammation—they are much more frequently the seat of simple hypertrophy, residual infection or hyperkeratosis of the epidermis overlying them.

These simple conditions are frequently viewed with great alarm, as they are interpreted as malignant disease. Attention is usully called to them during routine examination of the throat or mouth. Subjective symptoms occur infrequently and only when they are the seat of residual infection. Occasionally patients who are in the habit of looking at their tongues become aware of their presence and become greatly alarmed by finding these lesser or greater lumps.

I have made it a point to observe them for some time on routine examinations of the tongue. Mostly they protrude but slightly from the margin of the organ at the root; the opening of the crypt is small under normal conditions. As they are part of the lymphoid structure of the body, they are not infrequently found enlarged in patients in whom generalized lymphoid hypertrophy occurs.

Dissimilarity in size or an increase in the aperture of the cryptic opening, which may become deep and fissure-like, calls for careful examination. In the latter instance it is not infrequent to find that a semisolid, cheesy material can be expressed from the crypt; in several instances I have noticed an offensive odor associated with it. One such example is noteworthy to record because the patient's chief complaint was fetor ex ore. Only the left lingual tonsil was enlarged sufficiently to widen the crypt. Removal of the tonsil-bearing area of this side of the tongue improved the condition.

Subjective symptoms do occur in conjunction with residual or chronic infection. Especially is this true if the opening is insufficient to permit the easy outflow of the purulent material. At times this leads to fairly marked tenderness; the symptoms are usually exaggerated on mastication.

Three cases are presented briefly to illustrate some of the points in question:

CASE 1.—W. L. F., a man, aged 36, was sent to me by a laryngologist with a diagnosis of early carcinoma of the tongue at the margin. Examination showed the right lingual tonsil somewhat larger than the left, but the crypt was not distended. The mucous membrane covering a portion of it showed a grayish white plaque about 1 mm. in diameter, over which it seemed to be thickened. The rest of the mucous membrane covering the lingual tonsil looked macerated. There were no subjective

Fig. 1 (case 1).—Acanthosis overlying the mass of lymphoid structure underneath it.

symptoms. This abnormality was noticed during a routine throat examination. The entire tonsil-bearing area was removed by radio knife cautery.

Microscopic examination showed a normal lingual tonsil and hyperkeratosis of the epidermis overlying it. In figure 1 the slight acanthosis is shown overlying the mass of lymphoid structure underneath it.

CASE 2.—Mrs. W. W., aged 42, presented herself for examination on account of pain and tenderness at the left side of the tongue. The left lingual tonsil was somewhat larger than the right and was firmer in consistency. The opening of the crypt was patulous or distended. The area was very sensitive. No roughness of the teeth was noted. The entire area was removed by radio knife cautery. Microscopic section showed, in addition to a fairly large lymphoid structure, the presence of inflammatory exudate about the periphery and intracellular edema. It was interpreted as a chronic (residual) infection of the lingual tonsil.

CASE 3.—Mrs. G. B., aged 48, was referred to me because of a bilateral enlargement at the root of the tongue. The medical history was interesting because of a frequently recurring tonsillitis, which she had suffered over a period of the last ten years.

Figures 2 and 3 demonstrate clearly what was found. On the right side a lobulated mass, soft but not friable, was pro-

5. Perusse, G. L., Jr.: The Solution of Choice in Proctoclysis, Surg., Gynec. & Obst. 54:774-784 (May) 1932.

From the Pittsburgh Skin and Cancer Foundation.

1. Maximow, A. A.: A Textbook of Histology, edited by William Bloom, Philadelphia, W. B. Saunders Company, 1931, p. 483.

2. Boyd, William: A Textbook of Pathology, Philadelphia, Lea & Febiger, 1933, p. 436.

truding well beyond the margin of the tongue. On the left side a deep fissure separated the hypertrophied lingual tonsil and appeared as a deep cleft. A marked fetor ex ore was present, apparently coming from the left side. The lesions were destroyed by electrocoagulation.

DIFFERENTIAL DIAGNOSIS

As already mentioned and as in all chronic and persistent abnormalities of the oral mucosa, carcinoma, syphilis, tuber-

Fig. 2 (case 3).—Hypertrophy of the right lingual tonsil.

culosis, irritation from a rough or jagged tooth and irritation from tobacco, especially if the latter is used in the form of chewing, are the foremost considerations. Without going into the minutiae of detail, in general the following points will lead one straight: The absence of (*a*) hardness, as in carcinoma; (*b*) progressive or retrogressive changing character, as in a syphilitic gumma; (*c*) satellite lymph node enlargement, as in

Fig. 3 (case 3).—Hypertrophy of the left lingual tonsil, showing deep fissure-like crypt.

a chancre; (*d*) slow progressive ulceration quality, as in tuberculosis (unless the residual infection is due to the Koch bacillus).

If there is doubt, however, the tonsil-bearing area can be easily removed under local anesthesia. The radio knife cautery simplifies the procedure. A microscopic examination will then usually clear up the diagnosis.

SUMMARY

1. The three cases of lingual tonsils reported here illustrate certain common disorders found in them.

2. In looking for causes of fetor ex ore, residual infection in the lingual tonsil should be considered as a possibility.

631 Jenkins Building.

AUTOMATIC HYPODERMIC SYRINGE FOR SELF ADMINISTRATION OF INSULIN AND OTHER USES

HERBERT BUSHER, M.D., ST. PAUL

The greatest drawback in the treatment of diabetes with insulin, encountered in active practice, is the necessity of the patient to administer this medication himself with a hypodermic needle. The instinct of self preservation creates in every human being a fear to inflict pain on himself. Many a sufferer from diabetes struggles along on diet, to his own detriment and to the chagrin of his physician, simply because he lacks the will power necessary to overcome this natural inhibition.

To overcome this difficulty I have devised an automatic hypodermic syringe. The device holds the syringe under ten-

Fig. 1.—Automatic hypodermic syringe.

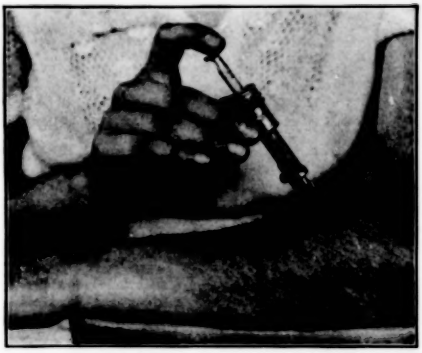

Fig. 2.—Method of use.

sion by means of a spring. After the syringe has been filled with the required amount of insulin, it is drawn back and cocked. The device is then placed firmly against the skin, and by touching a trigger the needle is thrust through the skin with lightning rapidity, very much as the modern spring lancet punctures the lobe of the ear in obtaining a drop of blood for laboratory examination. The rapidity with which the needle is inserted precludes any distortion of the skin, and therefore makes the procedure practically painless. Also, the spring-power insertion eliminates the voluntary push with its attendant inhibitory fear.

In addition to self administration there are other uses for which this device is well adapted. For instance, children will appreciate the painless injections not only in pediatric practice but also in the schools, where most of them receive their diphtheria immunizations.

The device has a foot-rest, which can be adjusted to the desired depth of needle insertion. The needle can readily be removed and another put on without unsterilizing it. And the syringe itself can easily be taken out of the device, and another syringe put in.

1071 New Lowry Building.

NEW APPARATUS FOR REHABILITATION FOLLOWING INJURIES TO THE LOWER EXTREMITIES

G. LYNN KRAUSE, M.D., ST. LOUIS

The after-care of patients recovering from fractures of the lower extremities has always been a considerable problem both to the patient and to the physician. From the time that the patient is ready to bear his weight on the lower extremities until his discharge he is constantly apprehensive of falling and disturbing the healing of the fracture. In order to remove these fears from his mind and to restore self confidence in his power of locomotion, I have devised an apparatus that has proved successful in a number of cases.

CONSTRUCTION AND USE OF THE APPARATUS

The apparatus consists of a framework of galvanized iron pipe joined together by tees and elbows. The base of the frame is 25 by 25 inches and is mounted on ball bearing rubber tired casters. It can be opened in front and wheeled up to the patient and then fastened. The upper framework is smaller than the base, measuring 20 by 20 inches and 35 inches from top of base to floor. Three sides of the frame are rigid; the fourth, or front, consists of a movable piece of pipe, which locks into place by a spring catch. The side opposite to this gate, or the back of the frame, is curved so as to accommodate the patient's hips and buttocks. The sides, to the right and left, are equipped with arm supports similar to those on crutches, and can be raised or lowered by set screws to fit the patient and help him to support himself during the early part of his rehabilitation. These crutch supports are in turn connected to the top framework by oversized tees, one on each side, which act as hinges so that the crutch attachments may be folded on to the lower frame when the patient has learned to support himself well enough to do away with the arm supports. From the center of the gate in front to the center of the curved bar in the rear, a well padded canvas sling is suspended. This strap passes between the patient's legs and supports the entire body above the hips. This arrangement allows the feet to touch the ground, so that the patient can begin to move his limbs in the normal manner for walking and yet keeps the weight of his entire body off the injured limb. As he recovers his confidence and the injury becomes more secure, the strap between his legs is gradually lowered so as to place more and more weight on his feet. The casters allow him to "walk" about as he regains confidence and reeducates the muscles of his limbs. At first the patient uses the adjustable crutch supports under his arms, but, as he improves and bears more weight, these supports are folded to the sides. Since the base is wider than the top, it is impossible for the apparatus to tip over. The adjustability of crutch and sling will accommodate any adult patient.

Fig. 1.—Ambulatory crutch for certain disabilities of the lower extremities.

The apparatus is being used at present on a man, aged 54, weighing 228 pounds (103 Kg.). Both legs were broken at the knee joint in an automobile accident, the fracture extending into the joint; the femur, tibia and fibia were broken. After a fair amount of bony union had been obtained, I was unable to get him to use crutches. When I put him in this device he was able in a few days to walk from one to two blocks. The exercise afforded is rapidly bringing back the use of his joints and muscles. He has acquired his equilibrium and confidence in walking. Also there is no danger of falling and injuring the broken parts or incurring any additional injuries.

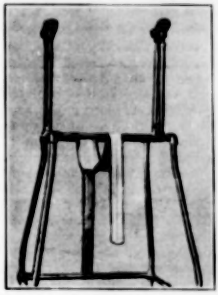

Fig. 2.—Detail of crutch.

With this apparatus the time the patient stays in bed is considerably shortened, which is a distinct advantage, particularly in elderly patients, in whom pneumonia is so prone to develop.

This apparatus can be used not only for fractures but also for rehabilitation in various forms of paralyses involving the lower extremities and in old cases of arthritis of the lower extremities, muscular dystrophies and atrophies, poliomyelitis, ankylosis and other conditions.

614 Beaumont Medical Building.

Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY OF THE AMERICAN MEDICAL ASSOCIATION HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORTS.

H. A. CARTER, Secretary.

THE McINTOSH ELECTRICAL CORPORATION AND THE AMERICAN COLLEGE OF PHYSICAL THERAPY

In THE JOURNAL, Sept. 23, 1933, page 999, the Council on Physical Therapy authorized publication of the report dealing with the American College of Physical Therapy, 5 North Wabash Avenue, Chicago. The purpose of this article was to inform the profession concerning the status of the so-called "College."

Several announcements of the "College" advertising the alleged postgraduate course and clinics in physical therapy were referred to the Council on Physical Therapy by physicians who had received them through the mail. In each case an announcement was attached to a piece of advertising matter of the McIntosh Electrical Corporation.

Two days after the aforementioned issue of THE JOURNAL was in print, a letter was received from the McIntosh Electrical Corporation by the secretary of the Council on Physical Therapy. In this letter the McIntosh Corporation definitely denied any present affiliation with the American College of Physical Therapy. The Council on Physical Therapy takes this opportunity to publish this statement of the McIntosh Electrical Corporation.

CIRCUMDUCTOR NOT ACCEPTABLE

The Circumductor is a mechanical exercising machine, manufactured by the Circumductor Corporation, Ltd., Los Angeles. The machine resembles an operating table equipped with extensions, levers, clamps and straps, to which the patient, lying on his back, may be fastened securely. Passive exercise is administered by means of various levers, which are moved or rotated through certain predetermined angles by an electric

motor. Arrangements are made also for so-called stretching of the muscles.

In the advertising matter propagandizing this unit, the firm makes this statement: "The Circumductor positively accomplishes the following:

"a. Equalization of tension of opposed sets of muscles.
"b. Relief of muscular congestion.
"c. Improvement of muscular tonus.
"d. Rebuilding of weak and unexercised muscles.
"e. Breaking down of muscular adhesions."

In the Council's investigation of the Circumductor, the promoters were requested to submit evidence to verify the therapeutic claims advanced. After giving careful consideration to such evidence as was made available, the Council declared it insufficient to justify the acceptance of the machine. Most of the reports received from those who have had experience with it were negative and, moreover, in noncritical reports recording optimistic views, only three or four cases were cited as evidence. One user believed that the machine produced a certain psychologic effect on patients, which effect he considered to have some value. The Council is of the opinion that psychologic effects may be produced more economically and scientifically than by a utilization of this machine.

Because of the lack of conclusive and critical evidence to substantiate the therapeutic efficacy of the claims made and because the safety of the unit is questioned, the Council decided to omit the Circumductor from its list of accepted physical therapy devices.

Council on Pharmacy and Chemistry

NEW AND NONOFFICIAL REMEDIES

THE FOLLOWING ADDITIONAL ARTICLES HAVE BEEN ACCEPTED AS CONFORMING TO THE RULES OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION FOR ADMISSION TO NEW AND NONOFFICIAL REMEDIES. A COPY OF THE RULES ON WHICH THE COUNCIL BASES ITS ACTION WILL BE SENT ON APPLICATION.

PAUL NICHOLAS LEECH, Secretary.

DEXTROSE (See New and Nonofficial Remedies, 1934, p. 270).

The following dosage forms have been accepted:

Sterile 2½% Dextrose in Physiological Sodium Chloride Solution in Vaculiter Container: Each 100 cc. contains dextrose, U. S. P., 2.62 Gm. and sodium chloride, 0.85 Gm.

Prepared by Don Baxter Intravenous Products Corporation, Chicago (American Hospital Supply Corp., Chicago, eastern distributor).

Sterile 5% Dextrose in Physiological Sodium Chloride Solution in Vaculiter Container: Each 100 cc. contains dextrose, U. S. P., 5.25 Gm. and sodium chloride, 0.85 Gm.

Prepared by Don Baxter Intravenous Products Corporation, Chicago (American Hospital Supply Corp., Chicago, eastern distributor).

Sterile 7½% Dextrose in Physiological Sodium Chloride Solution in Vaculiter Container: Each 100 cc. contains dextrose, U. S. P., 7.85 Gm. and sodium chloride, 0.85 Gm.

Prepared by Don Baxter Intravenous Products Corporation, Chicago (American Hospital Supply Corp., Chicago, eastern distributor).

Sterile 10% Dextrose in Physiological Sodium Chloride Solution in Vaculiter Container: Each 100 cc. contains dextrose, U. S. P., 10.50 Gm. and sodium chloride, 0.85 Gm.

Prepared by Don Baxter Intravenous Products Corporation, Chicago (American Hospital Supply Corp., Chicago, eastern distributor).

REPORTS OF THE COUNCIL

THE COUNCIL HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT.

PAUL NICHOLAS LEECH, Secretary.

CYPRESS OIL-N. N. R. AND OIL OF CYPRESS-SCHIMMEL AND CO. OMITTED FROM N. N. R.

Cypress Oil, with the accepted brand, Oil of Cypress-Schimmel and Co. (Fritzsche Bros., Inc., distributor), was first included in New and Nonofficial Remedies in 1912 as a palliative preparation for use in whooping cough. With the expiration in 1933 of the current three year term of acceptance of the commercial preparation, the Council reviewed the evidence for the usefulness of the product. The firm's submitted advertising consisted of a reprint of a paper by Dr. O. Soltman in *Therapie der Gegenwart*, March, 1904. There appears to be little or no recognition of Cypress Oil in American or English books of pharmacology. There is brief mention of the drug in Pfaundler and Schlossman's Handbuch der Kinderheilkunde.

In the light of these considerations the Council concluded that there is no good reason for the continued inclusion of Cypress Oil in New and Nonofficial Remedies and voted to omit it with the accepted brand.

Committee on Foods

THE COMMITTEE HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORTS.

RAYMOND HERTWIG, Secretary.

NOT ACCEPTABLE

CURTISS BUTTERFINGER 1¢
CURTISS BUTTERFINGER SENIOR 5¢
THE CHOCOLATE-COVERED PEANUT BUTTER CONFECTION

The Curtiss Candy Company, Chicago, submitted to the Committee on Foods "Curtiss Butterfinger 1¢" and "Curtiss Butterfinger Senior 5¢," wrapped bar confections of chocolate-coated centers prepared from peanut butter, corn syrup, sucrose, skim milk powder, molasses, salt, baking soda and flavoring.

Manufacture.—The "center" is prepared by cooking the corn syrup, sucrose, skim milk solids, and molasses in a steam jacketed kettle until a definite temperature is reached. The steam is turned off; the other ingredients are mixed in, the total mass is pulled and honeycombed by machine, and is mechanically spun to a desired size and shape. The prepared centers are chocolate covered, artificially cooled, and wrapped.

Analysis (submitted by manufacturer).—

	per cent
Moisture	2.0
Ash	1.2
Fat (acid hydrolysis method)	23.3
Protein (N × 6.25)	10.6
Reducing sugars as dextrose	14.0
Sucrose (copper reduction method)	25.3
Crude fiber	0.4
Carbohydrates other than crude fiber (by difference)	62.5

Calories.—5 per gram; 142 per ounce.

Discussion of Name.—The name "Butterfinger" for a food article suggests the presence of butter as an important ingredient. In fact, the product contains no butter but peanut butter or ground peanuts. Foods containing butter and peanut butter respectively have greatly different nutritional values. The term "butter" used as a part of the trade name for a food article containing no butter is misinformative and misleading. Food names should be appropriate and conform to the nature of the foods. "Peanutbutter Finger" accompanied by some such descriptive statement as "Chocolate covered peanutbutter confection" is an appropriate name and designation for this product.

The manufacturer was informed of the Committee's criticisms and recommendations but has not demonstrated compliance. This product will therefore not be listed among the Committee's accepted foods.

NOT ACCEPTABLE

BA-BEE NON-ACIDITY BREAD

The Ba-Bee Pastry Shoppe, Erie, Pa., submitted to the Committee on Foods a white bread called both "Ba-Bee Non-Acidity Bread" and "Ba-Bee Acidity Bread," made by the straight dough method, having the following ingredients: patent flour, buttermilk, water, yeast, salt, dry skim milk, honey, cream of tartar, bicarbonate of soda and distilled vinegar (acetic acid).

Analysis (submitted by manufacturer).—

	per cent
Moisture	40.0
Ash	1.6
Fat (ether extraction method)	2.0
Protein (N × 6.25)	10.9
Crude fiber	0.5
Carbohydrates other than crude fiber (by difference)	45.0
Acidity as lactic acid	0.73

Discussion.—The submission to the Committee named the bread "Non-Acidity Bread"; a leaflet accompanying the loaf designated the product "Acidity Bread" and stated: "A White

Loaf produced under a new and scientific process. This bread will not increase weight or create Acidity in the stomach, as it does not contain any sugar or fat solids. . . . Try a loaf of this marvelous bread today. . . ."

The submission discloses that the bread is prepared in the usual manner and not by a "new and scientific process." The bread will "increase weight" and "create acidity" in the stomach just as do other breads. The claim the bread "does not contain any sugar or fat solids" apparently is intended to differentiate this bread incorrectly from other breads and thereby give greater plausibility to the absurd names and other false claims. There is no objection to appropriate quantities of fat and sugar in bread.

The bread names and advertising are deceptive, an attempt to convey fictitious quasimedicinal values to an ordinary food. This product, therefore, will not be listed among the Committee's accepted foods.

ACCEPTED FOODS

THE FOLLOWING PRODUCTS HAVE BEEN ACCEPTED BY THE COMMITTEE ON FOODS OF THE AMERICAN MEDICAL ASSOCIATION FOLLOWING ANY NECESSARY CORRECTIONS OF THE LABELS AND ADVERTISING TO CONFORM TO THE RULES AND REGULATIONS. THESE PRODUCTS ARE APPROVED FOR ADVERTISING IN THE PUBLICATIONS OF THE AMERICAN MEDICAL ASSOCIATION, AND FOR GENERAL PROMULGATION TO THE PUBLIC. THEY WILL BE INCLUDED IN THE BOOK OF ACCEPTED FOODS TO BE PUBLISHED BY THE AMERICAN MEDICAL ASSOCIATION.

RAYMOND HERTWIG, Secretary.

KREEMEX BUCKWHEAT AND WHEAT FLOUR

Manufacturer.—Allied Mills, Inc., Kreemex Cereal Division, Greenville, Ohio.

Description.—Self-rising flour mix containing buckwheat flour, standard patent flour, soya flour, dextrose, calcium acid phosphate, sodium bicarbonate, salt, corn flour and corn starch.

Manufacture.—Definite proportions of the formula ingredients are automatically mixed and packed in cartons.

Analysis (submitted by manufacturer).—

	per cent
Moisture	11.3
Ash	4.4
Fat (ether extraction method)	2.5
Protein (N × 6.25)	11.0
Crude fiber	1.3
Carbohydrates other than crude fiber (by difference)	69.5

Calories.—3.4 per gram; 97 per ounce.

VITAMIN D FORTIFIED PASTEURIZED MILKS

(1) ARISTOCRAT DAIRY PRODUCTS COMPANY'S
(2) CROWLEY'S
(3) DAIRYLAND
(4) EAST SIDE JERSEY DAIRY'S
(5) LYON'S
(6) MARIGOLD
(7) SUNSHINE DAIRY COMPANY'S
(8) BANQUET SELECTED
(9) CONSUMERS GOLD SEAL
(10) LINCOLN DAIRY'S
(11) MARION PURE MILK COMPANY'S
(12) MED-O-BLOOM

Distributors.—(1) Aristocrat Dairy Products Company, Atlanta, Ga. (2) Crowley's Milk Company, Inc., Binghamton, N. Y. (3) Southwest Dairy Products Company, Fort Worth, Texas. (4) East Side Jersey Dairy Company, Anderson, Ind. (5) Lyon Creamery Company, Ltd., Riverside, Calif. (6) Marigold Dairies, Inc., Rochester, Minn. (7) Sunshine Dairy Company, Milwaukee. (8) Banquet Ice Cream & Milk Company, Indianapolis. (9) The Consumers Dairy Company, Toledo, Ohio. (10) Lincoln Dairy Company, Hartford, Conn. (11) Marion Pure Milk Company, Marion, Ind. (12) Med-O-Bloom Dairy, Kokomo, Ind.

Description.—Bottled pasteurized milk fortified with vitamin D (vitamin D concentrate prepared from cod liver oil); contains 400 U. S. P. X (Revised, 1934) vitamin D units per quart.

Preparation.—The milk complies with legal requirements and is pasteurized by the standard holding method. See THE JOURNAL, July 1, 1933, page 34, for description of fortification with vitamin D.

Vitamins.—The vitamin D concentrate used and the fortified milk are regularly tested biologically. Clinical investigation shows this milk to be a reliable antirachitic agent.

Claims of Distributors.—A vitamin D fortified, antirachitic pasteurized milk having otherwise the natural flavor and food values of usual pasteurized milk.

IRRADIATED VITAMIN D PASTEURIZED MILK

(1) ANNETTE'S DAIRY'S
(2) BLOSSOM DAIRY COMPANY'S
(3) CLOVER LEAF-HARRIS
(4) GRAND RAPIDS CREAMERY COMPANY'S
(5) GRAND RAPIDS CREAMERY COMPANY'S GOLDEN JERSEY
(6) OLD TAVERN FARM'S
(7) PEVELY DAIRY COMPANY'S
(8) WORDEN'S

Distributors.—(1) Annette's Dairy, Savannah, Ga., (2) Blossom Dairy Company, Charleston, W. Va., (3) Clover Leaf-Harris Dairy, Salt Lake City, (4) and (5) Grand Rapids Creamery Company, Grand Rapids, Mich., (6) Old Tavern Farm, Inc., Portland, Maine, (7) Pevely Dairy Company, St. Louis, and (8) R. F. Worden & Sons, Inc., Waterbury, Conn.

Description.—Bottled pasteurized vitamin D milk irradiated with ultraviolet light (patent No. 1,680,818).

Preparation.—The milk complies with legal requirements and is pasteurized by the standard holding method. For description of irradiation, see THE JOURNAL, Oct. 7, 1933, p. 1155.

Vitamins.—Clinical investigation shows this milk to be a reliable antirachitic agent. Contains 135 U. S. P. X (Revised, 1934) vitamin D units per quart.

Claims of Distributors.—Irradiated antirachitic pasteurized milk having otherwise the natural flavor and food values of usual pasteurized milk.

McCORMICK'S BEE BRAND POULTRY SEASONING

Manufacturer.—McCormick and Company, Inc., Baltimore.

Description.—Spice mixture for seasoning poultry, including sage, thyme, marjoram, nutmeg and black pepper.

Manufacture.—Definite proportions of the spice ingredients, prepared as described for McCormick's Bee Brand Allspice (THE JOURNAL, Oct. 28, 1933, p. 1393), are mixed and automatically packed in tins.

Analysis (submitted by manufacturer).—

	per cent
Moisture	9.7
Total ash	10.1
Acid insoluble ash	2.5
Nonvolatile ether extract	7.7
Protein (N × 6.25)	12.9
Starch (diastase method)	0.4
Crude fiber	16.2
Carbohydrates other than crude fiber (by difference)	43.2

Claims of Manufacturer.—All ingredients conform to the definitions and standards of the United States Department of Agriculture.

BEWLEY'S BEST WHOLESOME WHOLE WHEAT FLOUR

Manufacturer.—Bewley Mills, Fort Worth, Texas.

Description.—Dark red hard winter whole wheat flour.

Manufacture.—The wheat is thoroughly cleaned, ground in a burr mill, redressed on a centrifugal reel, and packed in sacks.

Analysis (submitted by manufacturer).—

	per cent
Moisture	11.5
Ash	1.9
Fat (ether extraction method)	2.0
Protein (N × 5.7)	15.0
Crude fiber	2.0
Carbohydrates other than crude fiber (by difference)	67.6

Calories.—3.5 per gram; 99 per ounce.

Claims of Manufacturer.—A whole wheat flour conforming to the United States Department of Agriculture definition and standard.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, APRIL 7, 1934

DINITROPHENOL POISONING

In this issue of The Journal appear the reports of two cases of sudden death from poisoning with dinitrophenol (pp. 1141 and 1147). The authors review the available literature on the subject, which would seem to indicate that the drug is treacherous and that its administration, as has been previously emphasized in The Journal, should invariably be under the control of a physician. In the case reported by Drs. Poole and Haining a young woman secured for herself and took without medical instruction a dosage of this substance far beyond what has been established as a safe amount. In accordance with instructions placed on the label by the druggist from whom the preparation was purchased, the patient took 3 grains the first day, 6 grains the second day, 9 grains the third day, 12 grains on the fourth day, 12 grains on the fifth day, and possibly 6 grains on the sixth day. On the seventh day she died. Apparently an ordinary daily dosage of from 3 to 5 mg. per kilogram of body weight is a safe therapeutic dosage. The patient began with a daily dosage of 180 mg. and on the fifth day was taking 720 mg. Nevertheless, even these tremendous and obviously excessive doses were below the limit of what was thought to be the fatal dosage, based on animal experiments.

The investigators conclude that, as compared with animals, human beings have a more variable and an unpredictable susceptibility to dinitrophenol. While the literature on the subject, as far as concerns the use of this product on human beings, is not extensive, there is already evidence to indicate that the special susceptibility to the drug is far more frequent than drug sensitivity as applied to most other medical preparations.

As is usual with any drug used for cosmetic purposes, commercial interests have promptly entered the field of exploitation of dinitrophenol. There is not the slightest doubt that vast numbers of people are taking this preparation both with and without the advice of their physicians. At least two of the physicians who broadcast health information to the public through the radio and through the press have mentioned the use of this drug and have apparently failed to warn the public adequately concerning its dangers. Innumerable letters have poured into the headquarters of the American Medical Association asking for further information. Reports such as those here referred to should be taken as a definite warning of the toxicity and the special danger associated with dinitrophenol in some cases. Physicians who administer the drug to their patients should inform them thoroughly concerning such dangerous manifestations as increased temperature, severe urticaria and pruritus, and recommend immediate discontinuance of the preparation on the appearance of any symptoms of this character.

LOBAR PNEUMONIA

Knowledge of the pathogenesis of lobar pneumonia has reached a point that offers unusually promising angles for continued attack. That these possibilities are not being neglected is attested by three recent articles emphasizing different phases of the problem. Moreover, wide dissemination of the advances in knowledge of pneumonia are necessary, since most practitioners see relatively few cases during the course of a year. Thus, Sutliff and Finland [1] state that the number of cases of lobar pneumonia reported annually in Massachusetts is from 4,080 to 5,544, making perhaps one case a year for each of 6,595 practicing physicians.

Smillie and Leeder,[2] investigating the spread of pneumonia, have studied this problem by taking cultures of the nasopharynx in 264 contacts of 64 patients with lobar pneumonia due to types I and II pneumococci. The results indicate that about 20 per cent of the immediate family contacts of the patients harbored the homologous strain of pneumococci. Hospital contacts were rarely infected, however, and the Boston investigators therefore believe that it is justifiable to treat cases due to types I and II in open wards of general hospitals. The evidence studied suggests that there is some additional factor other than simple contact which determines the transfer of type I or II pneumococci from a patient with lobar pneumonia to contacts. Possibly colds may be the factor, or one of the factors, responsible. It was apparent that carriers of types I and II pneumococci may continue as carriers for a considerable period without giving rise to pneumonia in either the carrier or his contacts and without producing a second group of carriers.

Much stress has been placed on the early diagnosis of lobar pneumonia, especially since the advent of specific serum therapy. With a view to improving the ability to make early diagnoses and follow the course

1. Sutliff, W. D., and Finland, Maxwell: Type I Pneumococcic Infections with Especial Reference to Specific Serum Treatment, New England J. Med. **210**: 237 (Feb.) 1934.

2. Smillie, W. G., and Leeder, F. S.: Epidemiology of Lobar Pneumonia, Am. J. Pub. Health **25**: 129 (Feb.) 1934.

of the infection, Graeser, Wu and Robertson [3] studied forty cases of lobar pneumonia by means of serial daily roentgenograms and physical examinations. Comparison between these methods showed the roentgenogram to be the superior in detecting the early lesion and disclosing the extent of the process while the consolidation was developing. At the stage of maximum consolidation, however, the two methods were about equally informative. Visceral displacement could not usually be demonstrated by physical examination. When seen in the roentgenogram it was generally manifested as an elevation of the diaphragm on the affected side. In a few cases a slight shift of the mediastinum toward the lesion could be shown.

Type specific serum has found its greatest usefulness so far in lobar pneumonia due to the type I pneumococcus. Sutliff and Finland, in studying this matter further, find no room for doubt that concentrated type I antipneumococcus serum exerts a striking symptomatic effect and reduces the death rate by one half in type I lobar pneumonia in adults. They consider that the results which may be expected in patients treated before the end of ninety-six hours of illness are symptomatic change in two thirds of the recovered patients within thirty-six hours of beginning treatment, and a death rate of approximately 10 per cent. Again early diagnosis and prompt serum administration are emphasized. The high cost of potent serum, they consider, is a problem being gradually met by increased use and improvements in manufacture and distribution. In any case, the results are so valuable that the serum should be used regardless of cost.

SOME FACTORS IN WOUND HEALING

The rapidly growing knowledge of the manifold types of nutritional defects and their relation to human well being is beginning to influence almost every field of medical practice. Indeed, at present the investigation of the indispensable exogenous facts, such as the vitamins and certain inorganic compounds, and researches on the endogenous hormones, seem to vie with one another for consideration in the domain of practical therapy. Foods have become in the eyes of practitioners something more than mere carriers of energy. Glandular secretions and extracts, derived from tissues and organs distributed along the way from the pituitary to the gonads, are finding applications and experimental trial in a dozen unusual ways. As a medical writer remarked nearly a century ago, we have to cultivate a science and exercise an art.[1]

Much is being written about "growth promoters," an expression used most commonly to include some of the vitamins; but any essential ingredient of the diet is in truth a "growth promoter," for without it the normal development of a part or all of the organism is likely to be disturbed. From this standpoint, shortage of iodine or calcium or some unsaturated fatty acid (as has lately been contended) may be quite as disastrous as is the lack of one of the newly recognized vitamins. In the case of calcium or phosphorus, the presumable damage to developing teeth and their bony sockets is obvious to the dentist. The lack of iodine upsets the function of the thyroid gland and thus in turn the metabolism as a whole.

In many respects the processes of wound healing are comparable to those of growth. New tissue must sometimes be formed. Hence it becomes important to discover whether and, if so, in what respects repair processes in the body may be accelerated by special dietary measures. As recently stated,[2] malnourished patients must occasionally be subjected to surgical procedures, and often it is necessary to restrict the amount of diet after operation. Only too frequently does one observe the wounds of undernourished patients, particularly those of children, healing slowly and becoming infected. Unfortunately, it is not always possible in the clinic to establish the exact nature of a case of malnutrition or to determine the deficiency of the previous diet that produced it. So, too, it is quite impossible to tell whether a prolonged healing time of a wound is the result of malnutrition alone or of other causes more obscure.

For the present, these uncertainties can best be solved by recourse to animal experimentation. The studies of Harvey and his collaborators [2] are a step toward some of the solutions. They have shown that the rate of fibroplasia in "standardized wounds" of soft tissues, notably in the stomach wall, is surprisingly independent of the diet. In adult animals, for example, the rate of return of healing strength in wounds of the stomach was not appreciably affected by complete starvation, nor was it affected by giving half the required amount of an adequate diet over a short period. On the other hand, the healing of wounds in the stomachs of young rats was decidedly retarded by giving only half the required amount of an adequate diet. This retardation in healing of the wounds in the stomachs of young rats can possibly be explained by a reduction either separately or in combination of certain elements of the diet. The most probable elements are the vitamins, especially in relation to the deficiency of proteins and salts.

It is satisfying to learn the remarkable ability of wounds to heal in spite of great variations in the amount of food consumed. Evidently, under stress the body mobilizes its reserves in an effective way regardless of the intake. Perhaps this circumstance will help to explain the recent observation [3] that even marked interference with the circulation in the limbs need not retard the healing of fractures or other defects.

3. Graeser, J. B.; Wu, Ching, and Robertson, O. H.: Physical Signs and Roentgenographic Findings in Lobar Pneumonia in Adults, Arch. Int. Med. **53**: 249 (Feb.) 1934.

1. Latham's Lectures on Diseases of the Heart, 1845.

2. Howes, E. L.; Briggs, Harry; Shea, Richard, and Harvey, S. C.: Effect of Complete and Partial Starvation on the Rate of Fibroplasia in the Healing Wound, Arch. Surg. **27**: 846 (Nov.) 1933.

3. Key, J. A., and Walton, Frank: Healing of Fractures and Bone Defects After Venous Stasis, Arch. Surg. **27**: 935 (Nov.) 1933.

Current Comment

INSURANCE PRACTICE: ITS QUALITY AND ITS ECONOMICS

American physicians have become accustomed to seeing the effects of compulsory health insurance depicted in a roseate hue. Representatives of the foundations who would lure the American medical profession into greater and greater participation in the trend toward socialistic and state medical practice are wont to emphasize the increased emoluments of the medical profession under such systems. Insidiously they urge that the vast majority of physicians are not adequately paid for the service they render and that compulsory health insurance or some similar system will greatly enhance the incomes of medical men. In this connection the following quotation from the London *Lancet* [1] provides both information and argument:

> The deputation from the Insurance Acts Committee was received by the Minister of Health on March 8th, when Dr. Dain spoke of the hardship inflicted on many members of the profession by the 10 per cent cut on the 9s. capitation fee. This hardship is common knowledge amongst medical administrators although hardly realised by the public. Many insurance doctors have had to take their sons away from public schools as a result of this and other deductions. The quarterly cheque without the cut was often completely mortgaged before its arrival; ends hardly met then, so that the loss of ten pounds out of every hundred just made the difference, necessitating change of plans, of outlook, and often of environment. The national emergency which docked panel cheques also affected private practice. The patient who used to consult his doctor when not well learnt to go without medical attendance; others who used to be regular private patients went to hospitals; with the result that the receipts from private practice have fallen considerably in every area, and particularly in those industrial areas where unemployment is severe. The increasing number of doctors in private practice has made things still more difficult.
>
> The Minister could not promise the deputation that the cut would be removed, but he did promise that the profession would not be forgotten and that their 10 per cent should be restored if other people's were restored. This was really confirming the promise made by Mr. Neville Chamberlain when he was Minister of Health at the time the cut was imposed—namely, that as the profession had faced the situation created by the national emergency with such good grace he would see to it that when the emergency was over the capitation fee should be restored to normal at the earliest possible moment.

Turning from this enlightening paragraph, one finds another interesting point of view expressed in a discussion by Dr. Hugh Cabot [2] before the Association of American Medical Colleges. The proponents of state systems of practice have constantly asserted that the people generally in the countries in which such systems prevail get more and better medical service than is available to the majority of the American people. Dr. Hugh Cabot has at various times in his addresses before medical organizations expressed a highly social point of view. Nevertheless, his personal observation of medical practice is definitely in favor of the American system. Thus he says:

> A brief and cursory and, I think, perhaps careless study of the situation in five or six foreign countries in which my person and family have been involved has convinced me that there is no country in the world at the present time, unless it be England, in which the average American can receive the grade of medical attention which he has come to believe necessary. In other words, the medical service in many other countries is very well suited to the demands of those countries. I think, for instance, that Denmark is, perhaps, the outstanding country in which the people and the medical profession are very well adjusted to each other, but I am not at all prepared to assume that if we should transfer the precise conditions in Denmark to this country that anybody who properly represented the public would be satisfied with it.

1. Lancet **1**:600 (March 17) 1934.
2. Cabot, Hugh: J. A. Am. M. Colleges, January 1934, p. 34.

WILLIAM H. WELCH—TWO ANNIVERSARIES

On April 7, Dr. William H. Welch completes fifty years of continuous service to the Johns Hopkins University and to the Johns Hopkins Hospital; on April 8, he celebrates his eighty-fourth birthday. THE JOURNAL wishes to extend to Dr. Welch on this occasion its congratulations both on reaching this birthday and on his continuous interest in the problems of American medicine, from both the scientific and the social point of view. It is hoped that the coming years may give opportunity for a continuance of his earnest and sincere counsel.

SPECIES DIFFERENCES IN ORGANOTHERAPY FOR PERNICIOUS ANEMIA

It has long been known that, in addition to the hematologic and neurologic symptoms of pernicious anemia, the syndrome is characterized by gastric involvement. Indeed, it has been said [1] that achlorhydria is the usual accompaniment of the disease. The marked efficacy of beef, hog and horse liver as well as of desiccated whole stomach of the hog indicates that these tissues contain something which takes an important part in hematopoiesis but which, in the absence of normal gastric function, cannot be obtained from ordinary food materials. That this curative property does not reside in liver and stomach tissues of all species is apparent from some recent studies on the dog. Ivy, Morgan and Farrell [2] have demonstrated that total gastrectomy in this species is not regularly followed by anemia. In later studies [3] in which canine liver was used, the response with both the extract and the whole tissue led to the conclusion that, although the substance effective in pernicious anemia is present in dog's liver, the concentration there is only about one-fifth that in the livers of the other species commonly used in this connection. Likewise, when desiccated whole stomach of the dog was given to patients with pernicious anemia there failed to appear the typical signs of remission of the disease, despite the fact that all these persons responded in the usual way to the administration of horse liver. As total gastrectomy in the hog gives rise to an anemia [4] and hog liver is a potent therapeutic agent in pernicious anemia, it appears that gastric function in the dog does not play the same part in hematopoiesis that it does in certain other species.

1. Moschcowitz, Eli: The Relation of Achlorhydria to Pernicious Anemia, Arch. Int. Med. **48**:171 (Aug.) 1931.
2. Ivy, A. C.; Morgan, J. E., and Farrell, J. I.: Surg., Gynec. & Obst. **58**:611 (Nov.) 1931.
3. Strauss, M. B., and Castle, W. B.: Proc. Soc. Exper. Biol. & Med. **31**:360 (Dec.) 1933. Richter, O.; Ivy, A. C., and Meyer, A. F., ibid. **31**:550, 1934.
4. Maison, G. L., and Ivy, A. C.: Proc. Soc. Exper. Biol. & Med. **31**:554, 1934.

Association News

MEDICAL BROADCASTS

National Broadcasting Company

The American Medical Association broadcasts on a coast to coast network each Monday afternoon from 4 to 4:15 Central standard time (5 o'clock Eastern standard time, 3 o'clock Mountain standard time, and 2 o'clock Pacific standard time).

The next three broadcasts will be as follows:

April 9. Peculiar Accidents, W. W. Bauer, M.D.
April 16. Bird with a White Breast, W. W. Bauer, M.D.
April 23. Sanitation Goes Modern, W. W. Bauer, M.D.

Columbia Broadcasting System

The Association broadcasts on a Western network of the Columbia Broadcasting System each Thursday afternoon on the Educational Forum from 4:30 to 4:45 Central standard time. The next three broadcasts will be as follows:

April 12. Pretty Polly, W. W. Bauer, M.D.
April 19. More Health Delusions, W. W. Bauer, M.D.
April 26. Million-Murdering Death, W. W. Bauer, M.D.

ANNUAL CONGRESS ON MEDICAL EDUCATION, LICENSURE AND HOSPITALS

Thirtieth Annual Meeting, held in Chicago, Feb. 12 and 13, 1934

(Continued from page 1091)

DR. MERRITTE W. IRELAND, Washington, D. C., in the Chair

JOINT SESSION OF THE COUNCIL ON MEDICAL EDUCATION AND HOSPITALS AND THE AMERICAN CONFERENCE ON HOSPITAL SERVICE

Responsibility of the Hospital Trustee and the Relationship Between Trustees and Staff

HON. HOWARD S. CULLMAN, New York: Since, in voluntary hospitals, ultimate responsibility is vested in the board of trustees, the board must be aware of professional matters. That consciousness, however, need only include the appointment of a medical board in whom the trustees have full confidence. The trustees should relegate all professional questions to professional men, confining their activities to the lay aspects of hospital work. The average director feels that he is doing his bit if he helps raise money for actual maintenance charges or expansion programs. If directors, whom I assume to be able business men, familiarized themselves with the business policies of hospitals, I am convinced that there would be a minor revolution in many established practices. There are innumerable opportunities in the hospital field for the business man to perform a constructive function, if he will merely trouble to understand that function. A valuable cooperation between various institutions could be achieved in obtaining ambulance appropriations, in large scale purchasing arrangements, in organizing a system for training hospital executives, in discovering and publishing valuable facts on hospital, medical and nursing costs. many of the difficulties between municipalities and private hospitals would never arise if hospital trustees considered it a part of their function to act as lay ambassadors between the world of science and a somewhat bewildered public. All the authorities vested in the directors of a private hospital are, in the case of public institutions, properly within the province of a municipal, state or county department of hospitals. I can see no advantage in duplicating or dividing these functions. A board of directors that can serve no useful purpose is a potential menace.

Meddling in professional matters by laymen is pernicious. There is no surer way to undermine the morale of a medical board and disrupt an otherwise excellent service than for lay directors to suggest appointments or promotions to the professional staff. I am strongly opposed to members of the medical staff sitting on the board of trustees. I approve thoroughly of physicians sending their representatives to board meetings to present the professional point of view, but I do not believe that these representatives should have a voice or vote in the business management of the institution. I am convinced that the doctor-business man is either a second rate doctor or a second rate business man or both. It is unfair and unnecessary to burden a professional staff, whose scientific duties should command all its time and attention, with problems that can readily and advantageously be handled by laymen.

The relationship between a hospital board of trustees and the medical staff should closely parallel the relationship between the directors of a corporation and the technical staff—a business-like cooperation based on mutual confidence and mutual understanding.

DISCUSSION

DR. NATHANIEL W. FAXON, Rochester, N. Y.: The duties of the trustees are legislative rather than executive. They should refrain from directing administrative detail and should never interfere with strictly medical matters. Nevertheless, through proper organization they can not only keep themselves better informed regarding what is going on in their own hospital but they can also be of great assistance to the medical and administrative staff. All hospitals have three groups: (1) the trustees; (2) the administrative staff responsible for the running of affairs and coordinating the efforts of all; (3) the medical staff. Some hospitals have, and there is needed in all, a connecting group—an executive board representing the trustees, the medical staff and the administrators staff. The exact composition of this board is unimportant; there may be a majority of trustees or a majority of medical men; the essential point is a group in which the varied interests of the entire institution may be discussed, an agreement reached and reference made to the body having power to act. Trustees are the connecting link between indirect welfare, represented by hospital and medical care, and direct welfare, represented by the giving of food, clothing and shelter. There has always been a distinction between these two forms of charity. It is impossible to state accurately the amount of charitable work done by voluntary or private hospitals. The American Hospital Association, seeking to obtain at least a cross section of this work, compiled replies from 169 hospitals in nineteen states. These hospitals provided approximately ten million dollars' worth of free service to full charity patients—five million of this was paid for in some way—but the hospitals had to go in debt for the remaining five million. Here is a social financial problem for trustees.

SYMPOSIUM ON THE UNIVERSITY CLINIC

Size and Scope of a University Clinic

DR. HENRY S. HOUGHTON, Chicago: There are now not more than six or eight of all the medical schools in the United States and Canada that are not integrated with the structure, organization, methods and objectives of universities to which they are attached. Inevitably the training of physicians becomes more and more identified with the general field of higher education. The soundest formal education in medicine is the one that "makes the student the unit of education, not the course, the credit hours, nor the faculty." Nothing should induce us, however, to recede from educational standards that are demonstrably good, provided the means of attaining those standards are consistent with common sense, honesty and good will.

How large should a teaching clinic be? I can find no dependable criteria, no single or unitary standard, because of variations in forms of instruction. With amphitheater clinics and large group demonstrations, fewer patients are needed. With students in an apprentice relationship, taking active part in dignosis and professional care, more patients per student unit are required. Larger clinics, therefore, or fewer students, is the answer for this type of teaching. As between these alternatives, a reduction in students appears to be the logical course to advocate. Most of the difficulties now being experienced by practitioners, and most of the hard looks cast by organized medicine at teaching clinics, arise not alone from general economic disorders but also from overcrowding and maldistribution.

What field shall a university clinic cover? Definitions are difficult here, because of the varieties of structure and relationship that exist in different institutions. Even within the

category of tax-supported hospitals and clinics, under state or municipal control, there is great variation, from the Nebraska University Hospital in Omaha (no salaried teachers, no hospital charges) to the neighboring University of Iowa (where all members of the teaching staff are on salary, and more than 90 per cent are on the so-called full time basis) in which all classes of patients are admitted. The range in private teaching hospitals and clinics, endowed or substantially self sustaining, also is broad and includes on the one hand institutions like Cornell and the University of Chicago Clinics, which maintain pay clinics as a part of their teaching organization, and, on the other, organizations like Rush Medical College, which handles its outpatient teaching program through a charitable dispensary endowed for the care of the poor at a nominal charge or entirely free. It is possible to propose basic functions that should be served by these institutions:

(*a*) Educational and scientific. It is the business of a university in all its divisions to forward the acquisition and diffusion of knowledge. Its success will depend on the wisdom and skill of those who teach in it, and it is appropriate to measure its worth by these standards. This applies to clinical service, instruction and research quite as much as it does to economics or theology.

(*b*) Social functions. These premises have a special application in the care of the sick and the teaching of medicine. The leaders in clinical education are men of recognized professional skill, and their service cannot properly be denied to those who are able to pay for it. If these leaders are giving their undivided time to the university, some form of pay clinic results. If the university claims only a portion of their time, those who wish their service pay for it as a matter of private treaty. The result is the same, as a basic economic problem.

(*c*) Limitations. There are, however, natural boundaries in the scope of an instructional clinic conducted in this fashion. It is improper for a university to build up a clinical unit that shall exceed the needs of teaching and research. Whatever is necessary for purposes of study should be provided, but expansion beyond that point would represent an unsound educational and social policy.

The topic assigned to this symposium does not refer to it explicitly, but there is an implied query as to whether or not universities ought to maintain pay clinics for furnishing teaching material. The American Medical Association officially raises this question and has voiced its disapproval of the conduct of teaching clinics that utilize for instruction those who can and do pay a professional fee for the service rendered. It is appropriate to outline the structure and program of the University of Chicago Clinics:

(*a*) Student body. Not more than sixty-five undergraduate students in clinical studies can readily be accommodated, which is approximately the present enrolment. In addition, there is postdoctorate instruction, and a few students are taking other degrees than the doctorate in medicine.

(*b*) Formal instruction. This is given in apprentice form. A system of clerkships is employed. Groups are very small. There is intimate participation in the care of patients.

(*c*) Types of patients. There are three types: full pay, part pay and free. All are available for teaching. In 1932-1933 the total outpatient visits numbered 138,976; new admissions totaled 16,611. The clinic furnishes approximately 1.5 new patients per instructional day for medical students on service in that division, leaving out of account the advanced students who as interns and assistant residents rotate into the outpatient unit. Full pay patients were from 4 to 6 per cent of the total number. From 85 to 90 per cent of the patients paid something after careful investigation of their ability to pay by the admissions officers. Approximately 10 per cent were wholly free. Determination of capacity to pay is made by trained workers, after a detailed social history has been secured. In judging a patient's ability to pay, the family's resources are compared with the obligations brought by illness. In the inpatient service the picture alters perceptibly; 6.3 per cent during 1932-1933 paid the full rate; 63.0 per cent paid part of the cost of their hospitalization; 30.7 per cent were wholly free.

Two types of criticism of this theory and practice are voiced. One comes from those preoccupied with problems of medical economics, who contend that the clinics are being run for profit without reference to teaching needs, that they are making a great deal of money, and that they are damaging the practice of local physicians very much. The other criticism arises from those who look with disfavor on the educational program being followed.

Are the clinics being run for profit? It will suffice to point out that the annual, operating deficit in these two services is in excess of $200,000 annually (1932-1933, $254,058), covered by endowments and gifts (exclusive of affiliated institutions). No teaching clinic can be expected fully to carry its own costs.

Are the clinical teachers damaging the practice of local physicians? Very little. A survey made late in 1933 showed 32 per cent of the new admissions to be outside of Chicago altogether and 48 per cent outside of the local area of the clinics. The remainder constituted less than 0.8 per cent of the population of the district. Assuming that each of the new outpatients from the South Side paid $1.29 (which was the average paid by private, free and part pay taken together for the period under review), and that each patient made seven return calls at the same rate, each of the doctors practicing in the university outpatient department took $742 during the year out of the local district, the total population of which exceeds a million people. If, on the other hand, these instructors were in the private practice of medicine on the South Side, the competitive factor would be at least eight or ten times as great. This is the answer to the accusation so often made that the university is engaged in educating doctors and then taking their prospective clients away from them. In a practical sense the university clinical staff has been taken out of competition. The total of professional fees for all types of service rendered in outpatient and inpatient departments together was $1,060 in 1932-1933 for each full time physician who sees patients in the university, including the affiliated hospitals. Taking account again of charges of local competition, and deducting the percentage of patients coming from outside this area, the sum would be $551. If these men were in practice, the picture would be very different, as far as competitive practice is concerned. I am not including in any of these figures the number of patients actually referred by practicing physicians to the clinics, which is in excess of 7 per cent of the total number. In the six years of operation, the volume of patients has risen somewhere near to the optimum for purposes of teaching and study. People do not continue coming to a place that does not serve them properly, especially when they have to pay, if they are able to do so, as much as they would to any high class physician outside. No one can say that the system I have described is the best. It is in my judgment an important and highly significant experiment in medical education.

The disturbing issues that confront medicine in the United States are not the minor competitive element that exists in university clinics, like this, nor the abuses imputed to free clinics, but the much more difficult and baffling problems of selecting the proper number of the right kind of men to give society intelligent medical care at a fair cost, and of finding a way to distribute these men reasonably well throughout our population. Those in charge of teaching clinics are as alive to the perplexities of the situation as any one could be; they have no desire to contribute to the overloading of the profession by teaching great crowds of students, or to its economic distress by developing oversize clinics.

It is conceded that there is a competitive factor in clinics of the type under discussion, but if the competition is honorable it can properly be defended. It is fair and honorable (*a*) if conducted in accordance with the ethical regulations of the guild; (*b*) if charges are as carefully adjusted as they are in a high class private practice and are not below those asked by properly equipped private physicians; (*c*) if it does not expand beyond its obvious requirements for instruction and study.

The Teaching Clinic

DR. NATHAN B. VAN ETTEN, New York: The one organization that should control medical education in the United States is the one that represents the whole of the medical profession of the country. All special societies that divert the activities of physicians and weaken the power of the national

organization should confine themselves to the special exhibition of their special interests and give all their political strength to the organization that represents medicine in every corner of the land.

Standards of medical education should be those erected by the American Medical Association only, and the ethics of educational institutions should be the same as the personal ethics of every member of the association. Competitive practice of medicine by educational institutions should be eliminated as unfair employment of institutional prestige and advertised excellence in competition with individual physicians, who should have every freedom of opportunity which is their right.

The teaching clinic should be especially careful about competing for patients with their own graduates or with any practicing physicians. More than any other group, teachers are supposed to be exemplars in education and in ethical behavior, and they should subordinate personal ambition to strict adherence to rules of conduct which respect the professional privileges of others. I cannot see the slightest reason for restricting the activity of the university professor, provided there is no implication that he represents the institution in his private work. The really big man in medicine has not gained distinction from large fees but rather from the volume of his work, which has been attracted by the exhibition of unusual skill. The converse is the little soul whose vanity craves the satisfaction of material accumulation.

Competitive practice of medicine by an incorporated medical school or clinic is the corporate practice of medicine, is an operation of unsocial exclusion and combination bargaining, distinctly unprofessional. Such groups should be denied hospital privileges in tax supported institutions where the rights of the taxpaying physician must be protected. These groups are operating in restraint of individual opportunity and should be vigorously disapproved. The university clinic must never interfere in any way with the return of the patient to the practitioner. A large part of its educational function should be to help the practitioner and never to compete with him.

Some plan must be evolved to control the crowding into an already crowded profession of the two thousand or more American students now enrolled in foreign universities. Some international understandings should be attempted, since the economic distress of physicians seems to be no deterrent to those of our young people who are determined to become physicians.

The university clinic should provide clinical education in clinical centers in our large cities from which clinical knowledge might flow to the surrounding country, and to which practicing physicians may come for the continuing education which we all need all our lives. The scope of the university clinic should include postgraduate teaching of any physician in any specialty after he has qualified himself by a definite period of general experience. It would seem to be within the scope of the university clinic to extend graduate education through the medium of county medical societies by lectures supported by local clinicial demonstrations planned and executed by university faculties. Graduate teaching carried to the physician has been very irregularly offered but is keenly appreciated by him.

The Outpatient Clinic

DR. J. H. J. UPHAM, Columbus, Ohio: This article was published in full in THE JOURNAL, March 31, page 980.

DISCUSSION ON THE UNIVERSITY CLINIC

DR. JOHN WYCKOFF, New York: I think there can be no question that the medical student must work in a clinic. The first speaker neatly evaded saying how large that should be. Of course, I think none of us know. The school which I have the honor to serve has all the material and more than we need. We feel that to do adequate teaching we need six hospital beds for every clinical clerk, and we feel that we need two outpatient visits daily for every clinical clerk. Dr. Van Etten says that the patient should always be returned to the doctor. I don't believe that, if the "always" must be in there, it will be possible to teach medicine properly in a university clinic. Do we teach students only disease or do we teach students how patients react to disease? Certainly the patient in the ward which I have in Bellevue Hospital reacts to disease differently from the patient one sees in private practice, and, surely, one of the great failures in medical education in the past has been that the student has not had contact of late years with anything except one social stratum. I cannot see how we can produce the type of physician which the profession has a right to demand that we produce unless patients are studied who come from a different social stratum such as is found in a charity hospital. If the patient who comes to the university clinic always is returned to his physician, how, then, is the student to follow the course of ambulatory disease except in the type of patient who is the type of patient that he will probably himself never treat? The other statement which I should like to discuss is the last statement that Dr. Upham made. In talking of the pay clinic he seemed to feel that it had no place in undergraduate work. How is the student to be taught as an undergraduate that he must think of the patient's circumstances, if that opportunity is never given to him? It seems to me that it might be a good thing in a medical school to have undergraduate students work in a pay clinic. There was one thing that Dr. Houghton said, with which I feel I can agree, and that is that I doubt whether the university teacher and the university clinic are a true source of competition to the practitioner of medicine. I work in a medical school where we do not have full time clinical teachers. I work in a medical school where fifty years ago the clinical teachers were tremendously in competition with their graduates.

DR. AUSTIN A. HAYDEN, Chicago: I feel that I speak from, and maybe for, the 6,000 physicians of the metropolitan area of Chicago, whose offices and whose services have been through the period of this depression, as they have been through the periods of other catastrophes that have befallen the American people, always at the service of the people without regard for pay. The statement that Dr. Upham makes that the free outpatient clinic has become a recognized part of medical education, and a necessary part, goes without saying. That is the accepted way in which the clinical training can be delivered. The size and the scope of the clinic, from which this shall proceed, and the general character of it contain matters that are, as Dean Houghton admits, matters of controversy. According to a survey that was made by the Chicago Medical Society there are 1,000,000 clinic visits in the city of Chicago every year; at least there were in the last year. This number has been appreciably increased within the last year. In 1929 that number amounted perhaps to 600,000. There was no complaint at that time from any institution that that amount of clinical material was not sufficient for the clinical teaching that was to be done. As near as we can estimate, there are about 10,000,000 office visits in the city of Chicago annually, so that we believe that the total matter under discussion represents somewhere around 10 per cent of medical office practice. I do not blame Dr. Houghton for not more specifically stating that the size of a clinic will necessarily depend largely on the ideals of teaching and the objects of instruction that the head of the department has who is conducting that clinic. Dr. Houghton states that pay clinics have been criticized for being run for profit, without reference to teaching needs. He denies that. But I believe that his denial cannot be absolute. No one has ever said that the University of Chicago was making money out of the clinics that Dr. Houghton is conducting. But there has appeared in the conduct of the institution a deficit running in 1932 to $274,000, which, divided by 65, makes about a $4,000 deficit on every individual that goes through that school. The futility of this expenditure is emphasized by the fact that 80 per cent of the students who have the opportunity of this educational full time system that Dr. Houghton advocates, when it comes to a choice between a full time and a part time system of education in medicine, decide against Dr. Houghton's system and go to the West Side, to old Rush Medical College, to finish their medical instruction. It would seem that that is a useless use to put this money to. Dr. Houghton has stated that he believes that the use of fees derived from the patients that pay at the clinics of the University of Chicago are a proper source of income for the university, by which to cut down their deficit; in other words, that by paying doctors at the University of Chicago on a full time basis somewhere from $742 a year to the munificent sum of $1,060 a year, the fees of those medical men can properly be diverted to the eradication of the deficit

of the university in the operation of its clinics. He thinks that that is a tenable position; in fact, he says that it is fair. In the instance of the University of Chicago, no request has ever come to the society for the establishment of a clinic at the University of Chicago. It was not made known to the Chicago Medical Society, and only 6 per cent of the patients that Dr. Houghton has spoken of actually are referred to the clinic by practitioners. So I think the conclusion is justified that as an aid to the general practitioner the university clinic has not been a great help.

DR. IRVING S. CUTTER, Chicago: When the Ward Memorial Building was constructed, it was the judgment of the faculty that there should be a very strong emphasis placed on outpatient teaching. The question as to whether patients would be received in that clinic who could afford to pay a physician was distinctly answered, positively answered, in the negative. There is a careful social survey of every patient, so that under no possibility shall any patient be admitted who can afford to pay a physician. There are thousands of people in all the large cities who are unable to pay physicians and who lend themselves generously, willingly, for clinical teaching. Students are assigned to the several departments in this outpatient clinic so that they work there anywhere from four to six hours daily. I am sure that the clinic that does not take into consideration the human relations of every patient who comes to the clinic falls far short of the principal desirability to the teaching of medicine. It would be very easy for us to have a clinic where patients would be received who might pay more than others. It would be simple, and there would no doubt be a gain, each year, of possibly $100,000 or even more if that should be done. It is not done because we feel we have no right to receive any patient and charge that patient, if that patient is able to take care of his own personal medical responsibility. I have the feeling about the so-called free clinic that there is a tremendous increase in mendicancy and that a careless administration of free medical care is bound to result in a whirlwind to the medical profession unless proper safeguards are instituted. It is a good deal like the patient who comes in without a careful social survey and who is later found by the joint emergency relief to have thousands of dollars in the banks. The careful social survey is paramount. After it has been made certain the patient cannot afford to pay, the patient is entitled, somewhere, to genuine, sympathetic, skilful medical care. If it cannot be done in the clinics, the so-called free clinics, it must be done by the city or the county or the state, because that patient needs relief. If the faculty of Northwestern should assume that, because of the gift of a building and of adequate funds with which to equip that building with every modern medical appliance we had the right to charge these individuals as much as the private physician on the outside would charge them, I would feel that we had actually subverted the purpose of the gift. It is unfair that huge funds are solicited from philanthropists to set up great laboratories, clinics and hospitals and then actually enter on the practice of medicine in competition with the private individual. At Northwestern there are between 450 and 550 patient visits daily. That is an adequate number for the students we have to educate. I would not assume for a minute that, if we had 1,000 patients applying daily, we would admit them. We have reached the upper limit of our necessities and beyond that point we would assume that the patients applying for admission would have to be sent elsewhere. I think there are, on the average, about thirty to forty patients each day turned away by the clinic because it is found that they are able to pay a private physician. I am sure that no one of us has any specific point of divergence primarily from any of the authors, but I do feel that, viewing the thing in the broadest principle, from the broadest point of view, from the principle that, after all, the student becomes the doctor ultimately and that the plan under which he is trained influences his life thereafter—viewing the thing thus broadly, we must be very careful indeed that great endowments shall not subvert the student in his tendency thereafter in the practice of medicine. If we are to have general socialization of medicine, perhaps the clinics, some of them that have been mentioned, are wise and good. I doubt very much if that will ever occur. There is one thing quite aside from these papers and that is we have to educate honest men. We have got to educate students who are so fundamentally sound in the practice of medicine that temptation of no sort will swerve them from the direct path.

DR. REGINALD FITZ, Boston: One of the important things for teachers in any sort of a clinic to recognize is that, after all, the one really democratic thing in this country is disease. All people get sick. What we have to do is to bring up our students to realize that they must learn how to treat illness in a whole range of different sorts of people. It is unfortunate, if it should occur, that the medical student should be brought up with the idea that the treatment of pneumonia among poor people is any different from the treatment of pneumonia among wealthy people. Dr. Will Mayo said that any good doctor ought to consider himself a trustee of his patient's pocketbook. I wish that some scheme could be brought out by which students could have that taught to them more properly. Often, in teaching clinics, the teachers themselves encourage the students to spend money right and left, the idea being that the hospital happens to be so endowed that they can order tests ad infinitum. I should like to see taught more that the physician should spend the patient's money in the wisest possible way. It doesn't make one bit of difference in any given case whether a patient happens to have money or not; the point is that the student has to train himself to think that under no conditions is he going to waste anybody's money, that he has to learn to be economical, sensible and democratic.

DR. LANGLEY PORTER, San Francisco: It has been found that we can get the medical men's cooperation by recognizing that our duty does not end to the state as a medical school when we have graduated a group of well qualified young men to practice medicine. It is our duty to carry medical knowledge to the practitioner. This can easily be done. A few years ago 200 patients a year were referred to the state university medical school. Last year we had more than 3,000, and every month the number is growing. The doctor sends his patient, knowing that he is going to get back a full report on his patient and, furthermore, that he is going to be able to get any further advice he wants about that patient. The doctor is his own social service worker on that case. If a doctor says that a patient can pay nothing, or a third or half or all of the costs of x-ray and other expensive diagnostic procedures, we accept that as a statement. We don't go behind that. If the medical profession is not competent to do its own social service in such cases honestly, it isn't our business to question the integrity of the men who send us cases. That has been a very valuable thing. The only other point that was brought up that seemed sad was this constant emphasis on the difference between laboratory and clinical medicine. I thought that was dead many years ago. Clinical laboratory work is nothing more than an extension of ordinary methods of examination of the patient.

DR. C. R. BARDEEN, Madison, Wis.: When one talks in numbers instead of about individuals, there is always involved the question of the profession at large and the public at large, and the only way in which medicine can be satisfactorily practiced is through some sort of agreement as to the general policies in which both are represented. It is not fair to say that it is wholly a question of organized medicine to determine how medicine shall be practiced. The patient has as much to say about it as the physician. But the physician needs to educate the patient as to proper methods. I am strongly in accord with Dr. Lewis that the main thing to aim at is to train good family doctors. The family doctor is to be considered the primary basis of the profession. If that is the case, then we perhaps are overlooking his interest more than other interests in speaking so glibly of how fair it is to establish big public clinics and compete with the family doctor and protect the interests of the specialist. The great run of diseases are not outside the financial resources of the great run of people in normal times. I think that, if we are going to train family doctors, one of the first things we ought to think of is not competing too much with the kind of service he can best render.

DR. HENRY HOUGHTON, Chicago: This has been an extremely helpful discussion. The problem of pay clinics used for teaching purposes has had a number of wallops this afternoon, most of which I think have forwarded our thought.

When I said that I thought these clinics ought to be within the limits of the ethics of the guild, I meant exactly within the limitations of ethics of the American Medical Association, of organized medicine, and nothing else. There have to be clinics to teach in, one kind or another, and free clinics are potentially as great sources of abuse as any pay clinic could be. These things have to be watched and regulated. They have to be dealt with honestly, clearly and fairly. There are dangers on both sides. In the clinic that I discussed there has been an effort to keep it at the level that Dr. Wynckoff was talking about. I accept his figure of two patients, outpatient cases, daily per student as the ideal. We have not quite attained that ideal. The figure of six beds per clinical clerk we have accepted as being the proper ideal to reach. I have offered an interpretation of certain facts that are open for study. They are questions that arise out of a fundamental teaching educational policy of the University of Chicago, which have been of record for at least twenty years. There was one basic proposition, which I think is worthy of careful study; namely, that the income of physicians comes from the public, whether the physician practices directly and privately or indirectly through an institution. This is an inevitable part of the consideration of the use of pay clinics for educational purposes.

DR. AUSTIN A. HAYDEN, Chicago: I should like to say that I think the establishment of a well set up course in medical economics and perhaps medical history by a practicing physician is something that can be well considered by every medical school in the United States. The last thing I want to say is to the deans: I want to tell them that I think they have taken entirely too little interest in the problems of the practicing physician. When the student has been graduated by their institution, they have largely lost interest in him, or at least their interest has not been manifest by going to his meetings and learning his views. Only by the mutual exchange of ideas can the proper policies be shaped for the guiding of these institutions in the future.

(To be continued)

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION, PUBLIC HEALTH, ETC.)

ARKANSAS

Personal.—At the meeting of the Arkansas State Board of Health, January 18, Drs. Joseph G. Gladden, Western Grove, was named president; Thomas Wilson, Wynne, vice president, and William B. Grayson, Little Rock, secretary.

State Medical Meeting.—The fifty-ninth annual meeting of the Arkansas Medical Society will be held at Little Rock, April 16-18, under the presidency of Dr. Leonce J. Kosminsky, Texarkana, and with the Pulaski County Medical Society acting as host. Physicians participating in the program include:

Morris Fishbein, editor of THE JOURNAL, Chicago, The Trend of Medical Practice.
Shelby B. Hinkle, Little Rock, Progress in Obstetrics and Gynecology.
Arless A. Blair, Fort Smith, Childhood Tuberculosis.
Isaac G. Jones, De Queen, Conservative versus Radical Surgery.
Roy I. Millard, Dardanelle, Coronary Thrombosis.
John J. Shea, Memphis, Relationship of Allergy to Otolaryngology.
Ira F. Jones, Fort Smith, Uterine Hemorrhage.
Joseph G. Mitchell, El Dorado, Effects of Quinine on the Second and Eighth Nerves.
Oscar W. Bethea, New Orleans, Newer Developments of Physical Diagnosis.
Everett D. Plass, Iowa City, subject not announced.
George R. Siegel, Clarksville, Endocrine Therapy in the Climacteric.
William Decker Smith, Texarkana, Carcinoma of the Uterus.
Charles S. Holt, Fort Smith, Progress in Surgery.
Henry G. Rudner, Memphis, Symptoms and Treatment of Dysfunction of Colon.
Hillel Unterberg, St. Louis, The Psychoneuroses.
Roland M. Klemme, St. Louis, Trigeminal Neuralgia, Diagnosis and Treatment.
Solomon F. Hoge, Little Rock, Late Syphilis.
William T. Wootton, Hot Springs National Park, Allergy an Everyday Problem.

Dr. Fishbein will address also an evening session on "Fads and Quackery in Healing." The annual banquet and president's ball and reception will be held Tuesday evening.

CALIFORNIA

Health Departments Merge.—The San Leandro Health Department and the Alameda County Health Department have combined and will function under the direction of Dr. Ira O. Church, county health officer. Dr. Luther Michael retired as health officer of San Leandro, having held the position many years.

Deaths from Mushroom Poisoning.—With eighteen deaths within a week in California from mushroom poisoning, Dr. Jacob C. Geiger, health officer of San Francisco, issued a warning, March 3, advising all except botanical experts to avoid mushrooms unless their species and source are definitely known, it is reported. Dr. Geiger urged that consumers purchase their mushrooms from a certified source, pointing out that poisoning is seldom traced to commercial markets.

Professor Not Associated with "Anti-Narcotic League."—Dr. Clinton H. Thienes, professor of pharmacology, University of Southern California School of Medicine, states that he has no connection with an organization called "International White Cross, Anti-Narcotic League, Inc.," with headquarters in San Francisco. In a letter to the executive secretary of the organization he protests against the use of his name as a member of its advisory council on a pamphlet entitled "The Truth About the Narcotic Situation in the United States." Dr. Thienes states that he disapproves the contents of this pamphlet and asks that his name be removed from all literature and other matter prepared, written or sponsored by the organization.

CONNECTICUT

Society News.—At the quarterly meeting of the New Haven County Public Health Association in New Haven, March 1, the speakers were Dr. Herbert R. Edwards, acting health officer, on "Examination of Food Handlers"; Mr. Sidney G. Davidson, superintendent, Grace Hospital, "Hospital Charges and Other Problems as Related to Public Health," and Mr. Warren J. Scott, director, bureau of sanitary engineering, state department of health, "Various Methods of Sewage Treatment in Connecticut."

Health at Hartford.—Telegraphic reports to the U. S. Department of Commerce from eighty-six cities with a total population of 37 million, for the week ended March 24, indicate that the highest mortality rate (22.4) appears for Hartford, and for the group of cities as a whole, 12.5. The mortality rate for Hartford for the corresponding week last year was 10.9, and for the group of cities, 11.7. The annual rate for eighty-six cities for the twelve weeks of 1934 was 12.7, as against a rate of 12.3 for the corresponding period of the previous year. Caution should be used in the interpretation of these weekly figures, as they fluctuate widely. The fact that some cities are hospital centers for large areas outside the city limits or that they have a large Negro population may tend to increase the death rate.

DISTRICT OF COLUMBIA

Medical Bills in Congress.—S. 3186, introduced by Senator McCarran, Nevada, proposes to provide compensation for disability or death resulting from injury to employees in certain employments in the District of Columbia. The term "injury" is defined to include such occupational disease or infection as arises naturally out of employment or as naturally and unavoidably results from accidental injury. An injured employee is to be authorized to secure first aid when necessary "from any qualified physician." If the injured employee desires additional medical attention, he must submit a request therefor to the deputy commissioner, who is authorized by the bill to permit the employee to continue treatment under the physician who rendered first aid treatment, or may direct the employee to submit himself for an examination and/or treatment to a physician or a group of physicians chosen by the deputy commissioner.

GEORGIA

District Meetings.—The Fourth District Medical Society was addressed at LaGrange, February 7, among others, by Drs. Robert L. Carter, Thomaston, on "Tuberculosis and Its Surgical Treatment."——The Tenth District Medical Society devoted its meeting, February 14, in Augusta, to a series of clinics.——Dr. Allen H. Bunce, Atlanta, gave a paper before the First District Medical Society, March 21, on "Treatment of Chronic Infectious Arthritis."

Cancer Clinic.—The creation of the Atlanta Cancer Clinic for pay patients has been authorized, with headquarters in the Medical Building of the Georgia Baptist Hospital, Atlanta.

A diagnostic fee commensurate with the patient's circumstances will be charged, the funds to be used for the maintenance of the clinic. A written report giving the diagnosis and recommendations for treatment will be sent to the patient's physician. Each applicant for admission to the clinic must be accompanied by or bring a letter from his physician. When there is no family physician, a signed statement to that effect will be required. The clinic will have available 370 mg. of radium. Dr. James L. Campbell has been designated director of the clinic.

ILLINOIS

Illegal Practitioner Found Guilty.—Mr. S. J. Kuflewski, chief inspector of the Department of Registration and Education of the State of Illinois, reports that E. H. Bernard of Chicago was taken before Judge Helander of the municipal court, February 20, on the charge of practicing medicine without a license. Bernard pleaded guilty, was fined $100 and was sentenced to one year in the House of Correction.

Health Promotion Week.—April 29 to May 5 has been designated as "health promotion week" in Illinois. Tuesday of that week is to be observed as "Child Health Day" in accordance with a proclamation issued by President Roosevelt. Speakers may be secured without local cost either through the state department of public health or from the speakers' bureau of the Illinois State Medical Society, 185 North Wabash Avenue, Chicago.

Chicago

Personal.—A course on ocular muscles was given at Northwestern University Medical School, April 2-4, by Dr. Alfred Bielschowsky, professor of ophthalmology, University of Breslau, Breslau, Germany.

Rongetti in Another Penitentiary.—Amante Rongetti, who recently completed a term in Fort Leavenworth, Kan., is now serving a sentence of from one to fourteen years in the Illinois State Penitentiary at Joliet, having been convicted of manslaughter. He was received at Joliet, February 10. In his first trial, on the charge of causing a death through an illegal operation, Rongetti was sentenced to death, but at the second trial the supreme court committed him to the penitentiary for from one to fourteen years. Rongetti completed a three year sentence at Leavenworth, February 6, for violation of the Harrison Narcotic Act (THE JOURNAL, Nov. 7, 1931, p. 1393).

IOWA

Graduate Courses Sponsored by State Society.—The speakers' bureau of the Iowa State Medical Society inaugurated three courses on graduate medical education, recently. One on general therapeutics opened at Creston, February 21, continuing weekly until April 25. Out-of-state speakers participating in this course are Carl R. Moore, Ph.D., Drs. Paul Cannon, Clifford J. Barborka, Samuel M. Feinberg, George W. Hall, and Oliver S. Ormsby, all of Chicago; George B. Eusterman, Rochester, Minn., and Arthur L. Tatum, Madison, Wis. The course on neurology and psychiatry was initiated, March 1, at Oskaloosa, these weekly sessions ending May 3. Dr. Alfred W. Adson, Rochester, Minn., was the visiting speaker. Infectious diseases is the theme of the third course, which opened in Mount Pleasant, March 2. The concluding lecture in this weekly series will be May 4. One out-of-state speaker participated in this group, Dr. Fred W. Gaarde, Rochester.

KANSAS

Personal.—Dr. Fay E. Gaither, Lenora, has been appointed health officer of Norton County.——Dr. Eber Reeves has been named health officer of Decatur County.——Dr. Charles McKinley has been appointed physician at the state penitentiary, Lansing, succeeding Dr. Robert H. Moore, resigned.——Dr. Darrel L. Evans has been named health officer of Riley County, succeeding Dr. John R. Mathews, Manhattan, who has resigned to engage in private practice in Glenwood Springs, Colo. He had held the position since 1923.

KENTUCKY

Private Physicians to Immunize Children.—The Louisville city health department, under Dr. Hugh R. Leavell, has announced a new policy with respect to immunization of school children, under which all children whose parents are able to pay are to be sent to private physicians. Formerly all school children were immunized by the health department at public expense. In cooperation with the Jefferson County Medical Society, the department is arranging a policy of having patients pay for medical service according to their ability and the society is preparing a list of physicians willing to accept these "part pay" patients. Steps have recently been taken to readjust also the hospitalization of the county indigent, the entire budget relating to health and hospitalization having been transferred from the county welfare department to the health department. Dr. Ben Wilson Smock has recently been appointed assistant to Dr. John D. Trawick, county health officer, and comprehensive plans are under way for coordination of the city and county health departments.

Society News.—A symposium on the common infections was presented at a meeting of the Jefferson County Medical Society, March 5, by Drs. Charles Dwight Townes, Will R. Pryor, Auryne E. Bell and Karl N. Victor. Dr. William T. Pride, Memphis, Tenn., addressed the society, March 19, on "Gynoplastic Repairs of Old Lacerations at the Time of Delivery," under the auspices of the Louisville Obstetrical and Gynecological Society.——Drs. Louis Feid, Jr., and Clifford J. Straehley, Cincinnati, addressed the Mason County Medical Society, Maysville, February 14, on treatment of benign uterine hemorrhage and classification of heart diseases, respectively.

LOUISIANA

State Medical Meeting at Shreveport, April 10-12.—The fifty-fifth annual meeting of the Louisiana State Medical Society will be held at Shreveport, April 10-12, with headquarters at the Washington-Youree Hotel, and under the presidency of Dr. Carl A. Weiss, Baton Rouge. Included in the scientific program are the following physicians:

Joseph E. Knighton, Sr., Shreveport, The Failing Heart of Middle Life.
John H. Musser, New Orleans, Treatment of Cardiovascular Syphilis.
Emmerich Von Haam, New Orleans, Importance of Biopsy in the Diagnosis of Cancer.
Harold L. Kearney, New Orleans, Bronchoscopic Aspiration in the Treatment of Lung Suppuration.
Arthur A. Herold, Shreveport, Pathology: The Basis of Scientific Medicine.
Marion D. Hargrove, Shreveport, A Review of 112 Cases of Amebiasis.
Martha Eleanor Cook, Lake Charles, A Simplified Treatment of Infantile Diarrheas.
Charles W. Duval, New Orleans, The Host-Cell Reaction to Invasion by Bacillus of Leprosy.
Francis E. LeJeune, New Orleans, Hoarseness: Its Significance.
Dean Lewis, Baltimore, President, American Medical Association, Chicago, The Surgical Lesions of the Breast.
Leon J. Menville, New Orleans, Bone Tumors from a Radiologic Standpoint.
Peter Graffagnino, New Orleans, The Chronically Diseased Cervix as a Focus of Systemic Infection.
Alcee L. Peters, Monroe, Suppurative Otitis Media.
Rufus Jackson, Baton Rouge, Nonpurulent Accessory Sinusitis.
George A. Mayer, New Orleans, Hypotension in Relation to Toxemias in Pregnancy.
Leon F. Gray, Shreveport, Squint and Its Treatment.
Rudolph Matas, New Orleans, On Vascular Surgery in Louisiana: A Historical Review.
Wiley R. Buffington, New Orleans, Importance of Recent Advances in the Etiology and Treatment of Certain Conjunctival and Corneal Diseases to General Medicine.
Clifford F. Rutledge, Shreveport, Diagnosis and Treatment of Intussusception by Use of the Barium Enema Under Fluoroscopic Control.
Edward L. King, New Orleans, Induction of Labor by Medical as Contrasted with Surgical Methods.
George C. Battalora, New Orleans, Compression Fractures of the Spine.

MAINE

Society News.—Dr. Sidney C. Dalrymple, Newton, Mass., addressed the Cumberland County Medical Society, February 23, on "Correlation of Clinical and Pathological Findings in Bright's Disease."——The Portland Medical Club heard Dr. Henry P. Johnson discuss "Some Effects of Climatic Changes on the Mucous Membranes of the Upper Respiratory Tract," February 6.——Speakers before the Kennebec County Medical Society in Gardiner, February 15, included Drs. Bernhardt I. Wulff, Waterville, on "Intravenous Urography" and Frank B. Bull, Gardiner, "Blood Transfusions."——At a meeting of the Oxford County Medical Society in Rumford, February 23, Dr. Warren E. Kershner, Bath, spoke on physicians' liability insurance and mastoid problems in general practice.

MASSACHUSETTS

Dr. Irving Appointed Professor of Obstetrics.—Dr. Frederick Carpenter Irving has been appointed William Lambert Richardson professor of obstetrics at Harvard Medical School. He is the first incumbent of the chair, which was recently created under the will of Dr. Richardson, former professor of obstetrics and dean of the medical school. Dr. Richardson bequeathed $100,000 to endow the professorship and the Harvard Corporation voted to name it in his honor. Dr. Irving was born in Gouverneur, N. Y., in 1883. Graduating from Harvard Medical School in 1910, he engaged in practice in Boston the same year, and became affiliated with the school in a teaching capacity in 1922.

Society News.—Dr. Thomas J. O'Brien, Boston, addressed the South End Medical Club, March 20, on medical legislation. —At a meeting of the Middlesex East District Medical Society in Stoneham, March 14, Dr. William R. Morrison spoke on "Stomach Surgery."——The clinical and experimental observations on the effect of total thyroidectomy was the discussion before the Harvard Medical Society, March 13; speakers were Drs. Samuel A. Levine, Eugene C. Eppinger, Philip Shambaugh, Morton G. Brown, Max T. C. Schnitker and Elliott C. Cutler, and Margaret E. Sawyer, Ph.D.——Among the speakers before the New England Roentgen Ray Society, March 16, was Dr. Edward C. Vogt on "The Esophagus and Gastro-Intestinal Tract in Infants and Children."—Drs. Harry C. Solomon, Houston H. Merritt, Jr., and Merrill Moore conducted a symposium on neurosyphilis before the Boston Society of Psychiatry and Neurology, March 15, and Dr. Robert E. Fleming and Elmer Stotz, B.S., discussed "The Blood and Spinal Fluid Alcohol in Abstainers, Chronic Alcoholics and in the Psychoses."

MICHIGAN

Dinner to Dr. Kamperman.—Dr. George Kamperman, Detroit, was honored by a dinner, given by his former residents, February 20, to mark his fifteenth anniversary as head of the department of obstetrics and gynecology of Harper Hospital. Following the dinner, Dr. Owen C. Foster unveiled a large framed "photomontage," a composite photograph depicting characteristic Harper Hospital scenes which serve as a background for photographs of Dr. Kamperman and surgeons trained by him since his appointment. It now hangs in the obstetric club room of the hospital. Dr. Harold C. Mack presented a bound testimonial and guest book containing letters and photographs of former and present residents.

County Secretaries' Conference.—At the annual conference of the county secretaries of the Michigan State Medical Society in Ann Arbor, March 7, the following program was presented:

Reuben L. Kahn, Sc.D., Ann Arbor, Recent Developments in Immunology.
Dr. Carl E. Badgley, Detroit, Traumatic Surgery.
Dr. Cyrus C. Sturgis, Ann Arbor, Therapy in Anemias.
Dr. Charles L. Brown, Ann Arbor, Therapy Limitations in Hypertension.
Dr. Ledru O. Geib and Henry F. Vaughan, Dr.P.H., Detroit, Our Preventive Medicine Program.
Dr. James B. Bradley, Eaton Rapids, Legislation.
Dr. Louis LeFevre, Muskegon, County Society Program in the Care of Indigents.
Dr. James D. Bruce, Ann Arbor, Progress and Planning in Postgraduate Education.
Drs. LeFevre, John B. Jackson, Kalamazoo; Herbert E. Randall and Carl F. Moll, Flint; J. Milton Robb, Detroit; Richard R. Smith and Burton R. Corbus, Grand Rapids, Medical Problems and Policies.

In addition, Dr. Carl D. Camp, Ann Arbor, conducted a neurologic clinic.

MINNESOTA

Personal.—A farewell dinner was given in honor of Dr. Elmer C. Bartels, January 23, by fifty-five physicians of Duluth. Dr. Russell J. Moe was toastmaster. Dr. Bartels has since gone to Springfield, Ohio, to practice.—The University of Minnesota recently received a gift of $500,000 for the advancement of medical research from Drs. William J. and Charles H. Mayo, Rochester.

Dr. Allen Honored on Hundredth Birthday.—Dr. Wilson A. Allen, Rochester, was presented with a resolution of the Olmstead-Houston-Fillmore County Medical Society, congratulating him on his one hundredth birthday and creating for him, as a special honor, the title of emeritus member with the privilege of active membership, without payment of dues. A telegram offering congratulations was also received by Dr. Allen from President and Mrs. Roosevelt. Dr. Allen observed his birthday, March 6, but because he was confined in a hospital, no special celebration was held. The resolution points out that Dr. Allen has been a member of the Minnesota State Medical Association since its organization. A resolution was also adopted by the common council of the city of Rochester in recognition of Dr. Allen's centenary. Dr. Allen served as mayor of Rochester for one term, 1895-1896. He graduated from Hahnemann Medical College and Hospital, Chicago, in 1879.

MISSISSIPPI

Bill Introduced.—S. 500, to amend the law relating to privileged communications, proposes that a physician shall not be required to disclose such a communication in any "legal" proceeding unless the patient expressly waives the privilege at the time of the trial. The present law prohibits such a disclosure in any "civil" proceeding "except at the instance of the patient."

Society News.—Speakers before the Central Medical Society, February 6, included Drs. Robert B. McLean, Jackson, on "Urticaria and Angioneurotic Edema," and Robin Harris, "Association of Scintillating Scotoma and Nasal Accessory Sinus Disease."——The meeting of the Issaquena-Sharkey-Warren Counties Medical Society in Vicksburg, February 13, was devoted to a discussion of the common cold.

NEBRASKA

Society News.—A symposium on obstetrics was presented before the Cedar, Dakota, Dixon, Thurston and Wayne Counties Medical Society, Emerson, February 20, by Drs. Leo J. Killian, Wakefield; John Buis, Pender; Paul F. Siman, Wayne; Ralph C. Gramlich, Walthill; Stuart H. Cook and Glen E. Peters, Randolph.—At a meeting of the Sixth Councilor District Medical Society, Osceola, January 16, Omaha physicians presented addresses: Drs. Rodney W. Bliss, on peptic ulcer; Abram E. Bennett, traumatic encephalitis, and Charles A. Owens, Jr., transurethral resection.——Dr. Abraham Levinson, Chicago, addressed the Omaha-Douglas County Medical Society, Omaha, March 27, on diagnosis and treatment of meningitis. Three physicians of Council Bluffs, Iowa, addressed the society, March 13, as follows: Drs. Gorden N. Best, on "Chronic Obstruction of the Duodenum"; Maurice C. Hennessy, "Foreign Bodies Producing Bowel Obstruction" and Karl R. Werndorff, "Reconstruction of Function in Paralyzed Extremities."——Drs. Maurice E. Grier and Lloyd O. Hoffman, Omaha, addressed the Otoe County Medical Society, Nebraska City, April 9, on infections of the genital tract.

NEW JERSEY

Bill Passed.—A. 245 has passed the assembly, proposing to amend the dental practice act by authorizing the revocation of a license to practice dentistry, if the licentiate violates any of the rules or regulations which the state board of registration and examination in dentistry may hereafter adopt with respect to the practice of dentistry.

NEW YORK

Bill Passed.—A. 417 has passed the assembly, proposing to amend the pharmacy practice act by providing (1) that a drug shall be deemed to be misbranded within the meaning of the act if its package does not bear a statement of the percentage of barbituric acid contained therein, but (2) that the act shall not apply to the manufacture and sale of proprietary medicines, except those containing poisons, deleterious and/or habit-forming drugs and chemicals.

Bills Introduced.—A. 1926, to amend those provisions of the medical practice act relating to osteopathy, proposes (1) to designate osteopaths as "osteopathic physicians"; (2) to forbid licensed osteopaths to perform surgery with the use of instruments, except to cut the umbilical cord, to circumcise, to use forceps for delivery, to repair the perineum, to lance superficial abscesses and to repair skin lesions; and (3) to permit licensed osteopaths to use and prescribe narcotics, anesthetics, antiseptics, vaccines, antitoxins and serums. A. 1927, to amend the provisions of the medical practice act relating to osteopathy, proposes that a license to practice osteopathy (1) shall not permit the holder to perform surgery with the use of instruments, except to cut the umbilical cord, to circumcise, to use forceps for delivery, to repair the perineum, to lance superficial abscesses, and to repair skin lesions; and (2) shall permit the holder to use and prescribe metaphen, resorcinol, zinc oxide, hydrogen peroxide, mercurochrome, iodine, potassium permanganate, menthol, thymol, ichthyol, sulphur, alcohol, spiritus frumenti, colloidal silver compounds, silver salts, adrenalin, ephedrine, epinephrine, iodoform, bichloride of mercury, phenol, opium and its derivatives, cocaine and its salts, novocain, procaine, veronal, luminal, amytal and its sodium salts, chloroform, ether, nitrous oxide, ethyl chloride, avertin, butyn, toxoid, toxin-antitoxin, antitoxin, staphylococcus vaccine, streptococcus vaccine, polyvalent vaccine, autogenous vaccine, pneumococcus vaccine, tetanus antitoxin, typhoid vaccine, neoiopax and tetraiodophenolphthalein for use in x-ray diagnosis.

New York City

New Members of Board of Health.—Dr. Haven Emerson, professor of public health administration, Columbia University College of Physicians and Surgeons, and Dr. Frank L. Babbott, Jr., president of Long Island Medical College, Brook-

lyn, were appointed members of the board of health by Mayor La Guardia in February. Dr. Emerson was health commissioner of New York from 1915 to 1918. The new members succeed Drs. Harry P. Swift and Rand Percy Crandall.

Salmon Lectures.—Dr. Charles Macfie Campbell, professor of psychiatry, Harvard University Medical School, Boston, will deliver the 1934 series of Salmon Lectures at the Academy of Medicine, April 13, 20 and 27 (THE JOURNAL, January 27, p. 300). The title of the first lecture will be "Trends in Psychiatry"; the second, "Classification Versus Dynamic Analysis," and the third will embody conclusions and suggestions.

Committee to Promote Sanitary Dispensing of Foods.—There has been organized in New York a Committee for the Study and Promotion of the Sanitary Dispensing of Food and Drinks, the purpose of which is to educate the public to demand sanitary practices in the dispensing of food and drinks in public eating places. Dr. Alec N. Thomson is chairman and Homer N. Calver, former editor of the *American Journal of Public Health*, is executive officer. The committee urges the public to protest to the management against all insanitary practices observed, to commend the management of places that uphold high sanitary standards and to report by name and address to the board of health all public eating places violating high standards.

Society News.—Speakers at a meeting of the Medical Society of the County of New York, February 26, were Drs. Thomas Francis, Jr., on "Diagnosis and Treatment of Influenza"; Henry T. Chickering, "Prognosis and Treatment of Lobar Pneumonia," and George G. Ornstein, "Pulmonary Atelectasis."——Dr. Boris M. Fried, among others, addressed the New York Pathological Society, February 22, on "Allergic Inflammation of the Lungs."——A symposium on "Indications for Roentgenotherapy in Malignant Disease of the Ear, Nose and Throat" constituted the program of the New York Roentgen Society, February 19; speakers were Drs. Maurice Lenz, Arthur P. Stout, Alfred A. Schwartz, John D. Kernan, Jr., Robert E. Buckley and George H. Semken.——A symposium on acute and chronic empyema was presented before the New York Surgical Society, March 14, by Drs. John F. Connors, Harold Neuhof, Adrian V. S. Lambert and Walton Martin.——The staff of Memorial Hospital presented a symposium on gastro-intestinal tumors before the Society for the Advancement of Gastro-Enterology, February 28; among the speakers were Drs. James Ewing, Lloyd F. Craver and George T. Pack and Edith Quimby, associate physicist.——Drs. William B. Castle, Boston, and Robert L. Moorhead addressed the Medical Society of the County of Kings, February 20, on "Modern Concepts of Anemia and Its Treatment" and "Cancer of the Larynx—Importance of Early Diagnosis," respectively.——At a meeting of the International and Spanish Speaking Association of Physicians, Dentists and Pharmacists, January 19, speakers were Drs. Franz Groedel, Frankfort, Germany, on hydrotherapy; Burton T. Simpson, Buffalo, on radium therapy, and George Henry, on psychotherapy. Dr. Jacob M. Gershberg, who was reelected president, gave his official address on the life of Professor Ramón y Cajal of the University of Madrid. At the February meeting a symposium on gastroenterology was presented, with the following speakers: Drs. L. Lee MacPhee, Boston, Leopold Lichtwitz, and George E. Binkley, and John Oppie McCall, D.D.S.

PENNSYLVANIA

Ten Deaths from Psittacosis in Pittsburgh.—At least ten deaths and several cases of psittacosis recently occurred in Pittsburgh as a result of contact with sick parrots in the pet department of a large department store. Psittacosis was first suspected when it became known that seven deaths had occurred among employees on only two floors of the store within two weeks, supposedly of pneumonia. A physician called to care for the eighth employee believed to have pneumonia had learned that the two floors of the store were decorated with parrots and parrakeets. He notified the city health department. Examination revealed that they had the disease and postmortem examination of the eighth patient from the store confirmed the diagnosis. The store in question immediately destroyed all its birds, discontinued the pet department and fumigated the store. All psittacine birds in the city were quarantined. The epidemic was traced to a shipment of 130 birds from California in January, of which three were dead on arrival, it was said. Dr. Lucius F. Badger of the U. S. Public Health Service went to Pittsburgh to conduct an investigation, March 17, after which he announced that the epidemic appeared to be under control. Later reports stated that two other pet shops had received shipments in which birds were sick or dead and that one case of psittacosis had been diagnosed from each shop. The San Francisco *Examiner* reported, March 17, that the California State Board of Health was investigating the report that some of the birds sent from California were shipped in violation of specific orders from the board.

Philadelphia

Gerhard Medal Awarded.—The Pathological Society of Philadelphia will award the William Wood Gerhard Gold Medal to Dr. George H. Whipple, dean of the University of Rochester School of Medicine and Dentistry, Rochester, N. Y., at a meeting April 12. Dr. Whipple will deliver the annual Conversational Lecture of the society, his subject being "Regeneration of Hemoglobin and of Blood Plasma Proteins Controlled by Diet Factors."

Impostor Claims Relationship.—A man has recently circulated among physicians in Washington, D. C., claiming to be a brother of Dr. Joseph McFarland, Philadelphia, and asking financial aid, it is reported. His story was that he had run past a stop light and damaged the car of another person, for which he was arrested and fined $25, which took all his ready cash. He stated that unfortunately he was without identification, but knowing that pathologists would know his "brother," he took the liberty of asking aid. He is a slender man, with steel gray hair, slightly bald, about 60 years old, well dressed, and with several teeth missing in front. Dr. McFarland has no brother.

Society News.—Speakers who addressed the Philadelphia Academy of Surgery, March 5, were Drs. Robert H. Ivy and Lawrence Curtis, on "Experience with Newer Procedures in Surgery of the Cleft Palate," and Alexander Randall, "Advantages of Preoperative X-Rays in Kidney Tumor in Children."——Dr. Lyman G. Richards, Boston, addressed the Philadelphia Laryngological Society, March 6, on "Sinusitis in Children: Diagnosis and Treatment."——Drs. William C. von Glahn and Alwin M. Pappenheimer, New York, were guest speakers at the meeting of the Pathological Society of Philadelphia, March 8, on "Relation Between Rheumatic and Subacute Bacterial Endocarditis."——Dr. Gabriel Tucker, among others, addressed the Philadelphia Pediatric Society, March 13, on "Obstructive Dyspnea in Children."

WASHINGTON

Society News.—Dr. Andrew C. Ivy, Chicago, will be the guest speaker at the annual open meeting of the Tacoma Surgical Club, April 7. Dr. Ivy will lead a symposium on modern knowledge of the physiology of the gastro-intestinal tract and will speak in the evening on "Applied Physiology of the Alimentary Tract." Demonstrations will be held at Tacoma General Hospital.——Dr. Howard L. Updegraff, Los Angeles, addressed the King County Medical Society, Seattle, March 19, on "Methods of Reconstructive Surgery."

WISCONSIN

William Snow Miller Lecture.—Chauncey D. Leake, Ph.D., professor of pharmacology, University of California Medical School, San Francisco, delivered the eighth annual address under the William Snow Miller Lectureship at the University of Wisconsin, March 23. Dr. Leake's subject was "Relations of Medicine and Art."

Personal.—Dr. Gilbert E. Seaman, Milwaukee, has been appointed acting head of the Northern Hospital for the Insane, Winnebago, replacing Dr. Peter P. Bell, resigned.——Dr. William M. Sweemer, Milwaukee, celebrated his fiftieth anniversary in the practice of medicine, March 11. Dr. Sweemer was a founder of the old Milwaukee Medical College, now a part of Marquette University, and served as professor of diseases of children from 1894 to 1904.——Dr. Albert Schmidt, Liberty Grove, celebrated his ninetieth birthday in January; he was greeted by all the residents of the village.——Dr. James E. Newton was recently appointed mayor of Hudson.

Fifty Years in Practice.—Residents of Oostburg and the contiguous territory gave a reception and banquet, February 20, in honor of Dr. Edward Was, who has practiced fifty years in the community. Dr. Was, a native of The Netherlands, graduated from Rush Medical College, Chicago, in 1884 and began practice in Oostburg immediately. Speakers at the banquet included Drs. William H. Gunther, William Van Zanten, Otho A. Fiedler, Otto T. Gunther, Harry H. Heiden and J. P. Zohlen, all of Sheboygan; Emmett F. Guy, Oostburg; John E. Guy, Milwaukee; Anthony Voskuil, Cedar Grove, and Robert M. Nichols, Sheboygan Falls. A plaque was presented to Dr. Was, inscribed with the legend "Fifty Years of Faithful Service, 1884-1934, from the Village of Oostburg."

GENERAL

Journal for Digestive Diseases.—March 15 marked the first publication date of the *American Journal of Digestive Diseases and Nutrition*. The journal will be issued monthly from Fort Wayne, Ind. Dr. Frank Smithies, Chicago, is editor, and Dr. Beaumont S. Cornell, Fort Wayne, supervising editor.

Death Rate Among Policyholders.—The death rate for 1933 among the industrial policyholders of the Metropolitan Life Insurance Company in the United States and Canada was 8.02 per thousand, the lowest ever recorded for this group, this in spite of a sharp increase in January in deaths from influenza, and the principal degenerative diseases. Decreases took place in deaths from tuberculosis, pneumonia, conditions arising from pregnancy and childbirth, diphtheria, whooping cough and measles. The death rates for diarrhea and enteritis and for fatal machinery accidents showed no change from their previous low points reached in 1932. Cancer, heart disease and diabetes recorded higher mortalities than ever before, even when the fact is taken into account that a larger proportion of the insured group is now in the older age groups. Accidental deaths, especially automobile fatalities, increased, though the number of deaths of children as a result of automobile accidents has diminished. The 1933 mortality rate for falls was the highest in fifteen years.

Epidemics of Measles.—It has been estimated that 7,000 cases of measles have occurred in Washington, D. C., since January 1; eleven persons have died. This is said to be the heaviest epidemic since 1921 in the capital. Philadelphia newspapers reported, March 18, that 10,688 cases had been reported to the city health department since January 1, with forty deaths. Baltimore had 1,988 cases reported between January 1 and March 14. It was reported more than 2,500 cases had occurred in El Paso County, Texas, from January 1 to March 6, with fifty-six deaths. Fifteen members of the freshman class at Harvard University, Cambridge, Mass., were stricken, the New York *Times* reported, March 22. Other epidemics have been reported from the following towns: Toledo, Ohio, 700 cases during the first nine days of March; Springfield, Ill., 800 cases between February 1 and March 18; Chattanooga, Tenn., 310 cases in the first two weeks of March; Salt Lake City, Utah, 506 cases during the week preceding March 4. The U. S. Public Health Service reported that 30,806 cases had been reported from forty-six states during the week preceding March 4, compared with 14,081 for the corresponding week of 1933.

Society News.—Dr. James R. Garber, Birmingham, Ala., was elected president of the Southern Interurban Gynecological and Obstetrical Society at a meeting in Birmingham, February 17; Dr. Willard R. Cooke, Galveston, Texas, vice president, and Dr. James L. Seibold, Birmingham, secretary. Drs. Everett D. Plass, Iowa City, and George P. Muller, Philadelphia, were guest speakers.——The Society for the Study of Asthma and Allied Conditions will hold its spring meeting in Atlantic City, April 28.——The tenth annual scientific meeting of the American Heart Association will be held in Cleveland, June 12, at the Cleveland Hotel. The program will be devoted to arteriosclerotic heart disease. This association moved its headquarters, March 30, to the R C A Building, 50 West Fiftieth Street, New York. —— The congress of the Association of French-Speaking Physicians of North America is to be held in Quebec, August 27-29, in conjunction with the twenty-third session of the Association of Physicians of the French Language, which includes members from France and Belgium.——The American Association on Mental Deficiency will hold its annual meeting at the Hotel Waldorf-Astoria, New York, May 26-29. The afternoon session, May 29, will be held jointly with the American Psychiatric Association. Dr. Groves B. Smith, Godfrey, Ill., is secretary of the association.——Dr. Philip H. Kreuscher, Chicago, was elected president of the Northwest Regional Conference in St. Paul, Minn., February 25, succeeding Dr. Benjamin F. Bailey, Lincoln, Neb.

Medical Bills in Congress.—*Changes in Status:* The Independent Offices' Appropriation Bill, H. R. 6663, which has been passed by the House and the Senate over the veto of President Roosevelt (Public Law No. 141), provides, among other things, that any veteran not dishonorably discharged, suffering from disability, disease, or defect, who is in need of hospitalization or domiciliary care, and is unable to defray the necessary expenses therefor, shall be furnished such hospitalization or domiciliary care in any Veterans' Administration facility, within the limitations existing in such facilities, irrespective of whether the disability, disease, or defect was due to service. A statement under oath by the veteran on such form as may be prescribed by the Administrator of Veterans' Affairs must be accepted as conclusive proof of inability to defray necessary expenses. S. 2688 has been reported to the House, with recommendation that it pass. It validates payments made by disbursing officers of the army for the medical and hospital treatment of members of the Reserve Officers' Training Corps and of members of the Citizens' Military Training Camps who contracted disease in line of duty while en route to or from and while at camps of instruction. *Bills Introduced:* S. J. Res. 92, introduced by Senator O'Mahoney, Wyoming, proposes to create a commission to formulate a permanent national policy with respect to benefits for veterans and dependents of veterans. S. 3111, introduced by Senator McKellar, Tennessee, proposes to authorize the erection of a veterans' hospital in middle Tennessee. S. 3175, introduced by Senator Couzens, Michigan, proposes to authorize clinics to withdraw alcohol tax free. H. R. 8818, introduced by Representative Welch, California, proposes to extend the benefits of the United States Public Health Service to fishermen, trapmen, net tenders, and other persons subject to the laws relating to American seamen. H. R. 8846, introduced by Representative Dockweiler, California, proposes to provide an increase of compensation for certain veterans' widows.

Government Services

Veterans' Compensation Restored

Pensions or compensation to veterans whose benefits were reestablished by the passage, over the President's veto, of the Independent Offices' Appropriation Act for the fiscal year 1935, will be restored with the least possible delay, the Administrator of Veterans' Affairs has announced. The Veterans' Administration estimates that approximately 330,000 World War veterans, 180,600 Spanish-American War veterans, and 34,900 dependents of Spanish-American War veterans will be affected by the new legislation, at an increase in cost to taxpayers of approximately $83,000,000 annually. Any veteran not dishonorably discharged who suffers from disability, disease, or defect, and who is in need of hospitalization or domiciliary care, and who is unable to defray the necessary expenses therefor, is to be furnished such hospitalization or domiciliary care in any Veterans' Administration facility, within the limitations of such facilities, irrespective of whether the disease, disability, or defect was due to service. A statement under oath by the veteran must be accepted as conclusive evidence of inability to pay. Under section 200 of the World War Veterans' Act certain disabilities were declared presumptively to be of service origin. The Economy Act of March 20, 1933, severed the service connections based on presumptions. The new act reestablishes these presumptions. The new law also restores to veterans with service-connected disabilities the same rate of compensation that was payable to them prior to March 20, 1933, except that the rate paid to veterans whose disabilities are service connected by presumptions is to be 75 per cent of the rate paid prior to the date named. Veterans of the Spanish-American War, who entered service on or before August 12, 1898, and persons who served in the Boxer Rebellion or Philippine Insurrection, who were receiving pensions for disability or age, March 19, 1933, are entitled by the new law to receive not less than 75 per cent of the pension then being paid, subject to certain restrictions relating to the financial need of the veteran, and whether or not the veteran is hospitalized. All laws in effect March 19, 1933, granting monetary benefits to veterans of the Spanish-American War, including the Boxer Rebellion and the Philippine Insurrection, are reenacted in their entirety, subject to the limitations prescribed in the new law and to such reduction in pensions, not exceeding 25 per cent, as may hereafter be made. The provisions of section 213, World War Veterans Act, are reestablished, whereby a person who is injured as a result of training, hospitalization or medical or surgical treatment or examination is awarded compensation on the same basis as if the condition were incurred in the military or naval service. Hereafter, service-connected money benefits payable to veterans of the World War are to be entitled "compensation," not "pension." Former compensation rates paid to totally blind World War veterans are reestablished, except where the veteran is furnished hospital care by the government and except as to cases involving fraud, mistake or misrepresentation.

Foreign Letters

LONDON

(From Our Regular Correspondent)

March 10, 1934.

The Battle of the Barbiturates

The controversy that has arisen over the dangers of the use as hypnotics of the large group of derivatives of barbituric acid was mentioned in THE JOURNAL, February 10. It has been continued in the medical press to such an extent that it has been termed by the *Lancet* the "Battle of the Barbiturates." Sir William Willcox, who struck the note of warning, is still the protagonist on the side of danger. His experience as a toxicologist is unrivaled, but the leading psychiatrists oppose him. In the *Lancet* he repeats his warning that the barbiturates have a powerful action on the nervous system and that care is required in their repeated daily use. It is constantly brought to his knowledge that, in therapeutic doses, symptoms such as mental depression drowsiness, visual hallucinations, vertigo, ataxic gait, indistinct speech, squint, nystagmus and paralysis of the limbs are common results. Indeed, a complex of symptoms identical with those of cerebellar disease, posterolateral sclerosis, epidemic encephalitis, bulbar paralysis or meningitis may be produced. Professor Richards of Aberdeen has recently sent him notes of three cases in which loss of memory and automatism followed daily therapeutic doses of barbiturates, and, as a result, an excessive number of tablets was unconsciously taken. Sir William disputes the figure that out of 5,147 suicides in 1931 only 13 were due to barbiturates (THE JOURNAL, February 10, p. 468). In 1933 Sir William treated eighteen cases of dangerous poisoning. Most of the deaths occur in persons who have been taking the drugs in repeated daily doses. He fully admits their value in the treatment of mental disorder.

Sir James Purves-Stewart, a neurologist, has observed three cases of paralytic syndromes of the mesencephalic, cerebellar and spinal type, respectively, following chronic use of barbiturates in therapeutic doses for hypnotic purposes. Other correspondents give further evidence of the increase of cases of poisoning due to barbiturates. From 1909 to 1914 there were admitted into the hospitals in Budapest thirty-five cases of barbital poisoning, but in 1932 there were admitted into one hospital of that city eighty-seven cases of barbital poisoning, and in addition phenobarbital had appeared on the list and was responsible for eighty cases. The argument on the other side is that the barbiturates have been used with safety and good results in an enormous number of cases. Sir Maurice Craig, a psychiatrist, wishes that Willcox had a few years' experience in the treatment of mental disturbances, for he would then appreciate what prescribing for these patients entails. He also considers it satisfactory that the suicide rate and accidental death rate taken together for barbiturates do not exceed two thirds of 1 per cent of the suicide rate in the country.

Professor Richards uses the term "automatism" for the mental condition induced by the habitual taking of barbiturates, which is so dangerous and yet has never been stressed in publications on the subject. Knowledge for the need of another tablet seems to persist, while the memory is so affected by the drug that the patient does not realize that he has already satisfied the need and automatically repeats the dose at intervals.

The Tax on Insulin

A protest has been evoked by the imposition of a 33 per cent tax on imported insulin. In the house of commons, Commander Locker-Lampson described it as a mistake in morals as well as in medicine and a tax on poverty and disease. There were in this country 100,000 victims of diabetes whom this tax exploited. For the government, Mr. Shakespeare replied that our experience since the imposition duties had shown that they did not necessarily mean an increase of price. When insulin was first manufactured in this country in 1923 the price was $6 for 100 units. In 1933 two firms in this country were producing it at 48 cents and a third at 40 cents retail. After the imposition of a duty, the British price had been reduced; two firms were producing it at 44 cents and a third at 34. The price of the imported product had not risen in spite of the duty but remained at 34 cents. Insulin was cheaper in this country probably than in any other country in the world except, possibly, Scandinavia. Recently, representations were made by American and Canadian producers to British producers that if the price was reduced any more it would be impossible to compete and produce it at an economic level. The fall of British prices since the imposition of the duty can be explained as either due to further improvements in the method of manufacture or to the fact that the profit was so large as to allow the reduction. The fact that Danish insulin after paying the 33 per cent duty is sold at the same price as the lowest British insulin shows that in the absence of a duty insulin could be sold at 33 per cent less than the present price. The minister expressed surprise that the Danish insulin was not made dearer by the duty but continued to be sold at the lowest British price. Elementary economics would have told him that there cannot be two prices for the same article in the same market and that if the Danish continued to be sold it would have to conform to the British price. All the sophistries cannot hide the fact that the insulin tax is a method of preventing the fall in price and is wanted for this purpose by the British manufacturers. It seems impossible to get from the minister the price at which insulin is sold in Denmark, but according to the Manchester *Guardian* (the leading liberal paper in this country) 100 units could be bought there a few years ago for 23 cents.

Cysticercosis as a Cause of Epilepsy

At a meeting of the Royal Society of Tropical Medicine, Col. W. P. MacArthur, consulting physician to the British army, showed that many cases of epilepsy were due to cysticercosis of the brain, a most important advance. The president of the society, Sir Leonard Rogers, described the paper as "historic." About 100 soldiers are discharged every year from the British army because of epilepsy. For many years occasional cases of cyticercosis complicated by epilepsy have been observed, but their significance was missed until they were reviewed as a whole, when it was noticed that all these cases were examples of heavy infestation, with striking clinical signs, and that there was no admixture of milder forms of the disease. Colonel MacArthur propounded the theory that the lighter grades of infestation were included in the heterogeneous group of "epilepsy" mentioned. An inquiry to test this theory produced such strong confirmatory evidence that the war office about eighteen months ago ordered all cases of late developing epilepsy sent to the military hospital, Millbank, for special investigation. Colonel MacArthur has collected more than sixty military cases of cysticercosis, and twenty have been diagnosed at the hospital during 1933. In the great majority of cases there was no evidence of infestation at any time with the adult Taenia solium. In the minority the symptoms began while the patient was under treatment for tapeworm, or there was a latent period of several years between the complete expulsion of a worm and the development of clinical cysticercosis. There is always a larger number of palpable cysts than show themselves, for, when they eventually calcify and become visible in roentgenograms, more may be seen in one arm than can be palpated in the whole body. The cysts may be detected in the muscles or subcutaneous tissue of any part of the body. Their size, when

palpated in muscles, usually suggests that of a pea or hazelnut. In the brain the cysticercus becomes enclosed in a wall of sclerosed neuroglia. The death of the cysticercus is associated with increase in the quantity of fluid in the cysts, which therefore becomes tense. Colonel MacArthur holds that while alive cysticerci usually are tolerated by the host, but after their death they act as irritants. Surrounding the dead cysticercus the brain tissues are seen to be undergoing active degenerative change with marked cellular response. In the brain, degenerating tissue may extend for at least 5 mm. beyond the cysticercus. After the death of the cysticercus, about three years is required for the scolex to calcify.

Of the nervous manifestations of cysticercosis, epilepsy is the commonest. The fits may begin about the time the cysts are first detected or there may be a long latent period before the first fit. As the parasites may lodge in any part of the brain, any symptoms—motor, sensory or mental—of a focal lesion may be produced. The picture may be that of cerebral tumor, disseminated sclerosis or, if there is hyperinfestation, acute encephalitis.

The diagnosis of cysticercosis is usually missed, because of failure to think of the disease. The history may be suggestive—the onset of fits in an adult without evidence of familial or personal epileptic taint. Residence abroad increases the probability of cysticercosis. The most helpful sign is the presence of palpable cysts, for which the patient should be examined from head to foot. But even in cases of heavy infestation of the muscles the parasites may not be evident. To demonstrate the parasite, a cyst should be excised. Roentgenography may disclose calcifying cysts.

No medicinal treatment is curative. The large number of parasites found in the brain and their wide distribution do not encourage resort to surgery. The successful removal of cerebral cysts has been reported, but before cure is certain, time must be allowed for the other parasites in the brain to die, which may take years.

The Population Problem in India

Major General John Megaw, late director general of the Indian medical service and now president of the medical board, India Office, gave a lecture to the East India Association on "Health and Population in India." He said that India was now the most populous country in the world, and in the last decennial period the increase was 10.6 per cent. Unless some unexpected check was applied there would be 400 millions of persons in India in 1941. He did not advocate any particular form of population control, whether celibacy, delayed marriage or contraception. Each individual and community must decide as to the special method of control acceptable to them. What he advocated strongly was that the people should be instructed in the hard facts which had to be faced and told how other countries had dealt with them. Remedial action ought to be prepared after a thorough investigation of the case by the best brains in England and India. The root cause of the trouble was ignorance, and the remedy was education. The difficulty would be to prepare a sound working scheme for instruction in life planning in an effective and acceptable manner. The cinema and broadcasting could be made instruments of revolutionizing the life of the Indian peoples in a few years.

In 1800 the population of Great Britain was 9 millions, growth for four of five centuries before that time having been extremely slow. Today it was between 40 and 42 millions—far too many—and yet it had been possible to produce out of this narrow environment what he believed to be the healthiest nation in the world. This had been accomplished not so much because of medical science as because of social circumstances, which had been controlled by the government and by individual effort, combined with education.

PARIS

(From Our Regular Correspondent)

Feb. 14, 1934.

The Academy's Protests Against New Fiscal Rulings

To make up the deficit in the budget, parliament has introduced legislation designed to bring in more taxes and subjecting the liberal professions (physicians, lawyers, authors and artists) to closer surveillance. It is held that many members of these professions make insufficient declarations as to their taxable income, since there is no adequate control. Parliament has ruled that all members of the liberal professions shall be compelled to keep a record of their daily receipts, which tax officers shall have the right to examine. The physicians immediately objected that they would be violating the right to privileged communication if they revealed the names of their clients. The law has therefore authorized the physician to use a figure in place of the name of a client, the figures being recorded in another book, kept secret, while the physician is compelled to give his clients receipts for the sums paid, only the accepted figure appearing on the receipts. The law thus modified has been passed by the two houses of parliament, which hopes to collect 400,000,000 francs ($26,000,000), in this manner. The medical syndicates immediately raised energetic protests and emphasized that the substitution of a number for a name did not constitute sufficient protection of professional secrets. The Academy of Medicine took up the question. Professor Balthazard pointed out that an edict of parliament of 1750, still in force, formally declares that medicine is not a trade but a matter of science, devotion and sacrifice. The Academy thereupon passed unanimously the following resolution: "The Academy, wishing to join in the protests of the various medical groups against the new fiscal regulations imposed on the medical profession, and recalling that physicians consider themselves bound absolutely by the right of privileged communication, protests against the regulations that appear inapplicable and opposed to the spirit of social and human solidarity of the medical profession, which cannot in any wise be compared with a commercial profession." Previously, Messieurs Vanvertz, Bezançon and Siredy had, in turn, shown that the law was not feasible. A physician summoned in an emergency to a patient cannot always carry his receipt book with him. The fees demanded of clients vary, in the option of the physician, with their financial worth, so that controllers of the treasury would constantly be suspecting fraud.

Right of Injured Workmen to Refuse Operations

The question as to the right of a person who is injured in an occupational accident to refuse an intervention has been much discussed before the Society of Legal Medicine. The most competent members have been unable to reach an agreement on the subject. The fact is, the law is poorly worded and is susceptible of several interpretations. The society admits, however, that if an injured person whose condition might be improved by an intervention capable of diminishing his invalidity and consequently his benefits should refuse to accept such intervention, he would be liable to suffer a reduction of his compensation. The society accepts such a reduction as only natural when, during the course of treatment, the injured person is guilty of "an inexcusable wrongful act." The cases are unfortunately numerous in which persons injured in an accident, in order to secure larger compensation, voluntarily neglect their treatment. The insurance companies, thus damaged, use all their efforts to prove such fraudulent neglect. The courts in such cases have rendered contradictory decisions, for the bad faith of the injured person is often difficult to prove. Hence the insurance companies desire a more precise wording of the law, and the proper text of the law has been the subject of discussions before the Society of Legal Medicine. If the

approval of the society can be secured for the text of a law, it can be presented to parliament with such guaranties as would make it likely to be accepted, except by the socialists, who, as a matter of principle, always take the side of the workman. A preliminary text has been drawn up, which reads as follows: "If before the expiration of the time limits for revision (three years) the injured person refuses a benign operation, to be performed, for example, under local anesthesia (ethyl chloride) —an operation that, without risk, would improve the functional state, the disability compensation shall be diminished in such proportion as the expert shall decide and the courts shall approve, if they deem it advisable." Mr. Sée approved these conclusions in general but remarked that in parliament it would no doubt be contended that the law of 1898 defines the apportioned compensations as a contract recompense. Mr. Hugueney admitted that the abuses are much more frequent than is generally supposed but thought that a revision of the law is useless, since it already provides for a reduction of the benefits in case of "inexcusable wrongful act" on the part of the workman. Mr. Bourgeois held that the cost of the new operation should be paid by the employer, together with half of the injured man's salary during treatment. Mr. Hugueney responded that the costs would fall on the insurance companies, since they are benefited by having the compensation of the workman reduced. No definite conclusions have been reached as yet, owing to the difficulty of defining the expression "inexcusable wrongful act" of the workman.

Compulsory Antityphoid Vaccination

The Academy of Medicine, at the suggestion of Messieurs Vincent, Dopter and Léon Bernard, has adopted unanimously a resolution recommending that antityphoid and antiparatyphoid vaccination of all the personnel of the merchant marine be made compulsory. Cases of typhoid among this personnel are frequent, being in part the result of the impure water they drink, when on shore leave, in the small ports of France and foreign countries where hygienic supervision is defective. The incubation period being sometimes rather long, the diagnosis by the ship's physician is often erroneous, and the sailors, with a false diagnosis of "gastric disorder with fever," often go to their homes in rural districts and create foci of typhoid.

BERLIN

(From Our Regular Correspondent)

Feb. 12, 1934.

Control of Proposed Cancer Cures

The federal commission for the combating of cancer, in its new line-up, has expressed a willingness to test out the proposals that are made by physicians and laymen for the prevention, recognition and cure of cancerous diseases. This supervision will be carried out with the cooperation of the president of the federal bureau of health, the competent representative of the Prussian Medizinalverwaltung, and the head of the department of pharmacology at the University of Berlin. All proposals, including those that appear at once to be useless, will at least be registered. Those that appear to have some possible value will be discussed by the commission as a whole, and such suggestions as seem worthy of serious consideration will be placed in the hands of experts. Remedies, the application of which, after a preliminary test, offers any possibilities of success will be tried out in a series of experiments in institutions, and during that time no information will be given out to the inventors of procedures. They will not be permitted to visit the institutions where the trials are being conducted. Before such research is begun, they must sign a statement to the effect that they will not make, either publicly or privately, any claims to rights or prerogatives with respect to publications, based on the fact that such trials are being made at the instance of the federal commission for the combating of cancer. They must agree that, following this research, they will use solely the report, in unabbreviated and unemendated form, of the federal commission. If the producers and inventors do not accept these conditions or do not adhere to them, or refuse to impart the information needed for the trials, the research will immediately be discontinued. In conducting such experiments, especial value will be attached to the securing of cancer cases that lend themselves to the drawing of comparisons. The hospital record card for tumor patients, which has been elaborated by the federal commission, will be made the basis for the selection of suitable cases.

Fundamental Changes in German Hygiene

Before the Berlin Medical Society, Professor Zeiss, the recently appointed hygienist of Berlin, delivered an address on "The National Tasks of German Hygiene." With the national revolution, he pointed out, the objectives and tasks of hygiene have been modified. In fact, a fundamental change of views has occurred. Whereas, under the former régime, the main emphasis in hygiene was placed on social welfare aid, today the principles of demographic science, which has, of late, received new impulses, must be more vigorously and actively applied. Thus, hygiene, more than ever, has become the center for a number of related fields. The hygienist is especially fitted to become the exponent of true racial research. He is "the natural diplomat of the physicians." The old conceptions of hygiene are outmoded. The old points of view of social hygiene must be abandoned. Fifty per cent of the program in this field must be omitted. Many branches of hygiene have, moreover, developed into well controlled special fields with their own technic; for example, street cleaning and sewage disposal. However, the division of hygiene into special branches is to be condemned. It is important to consider and to carry on hygiene as an indivisible whole. Medical students must, however, become familiar with fields hitherto entirely neglected; for example, with the problem of Germans living in scattered groups in foreign countries, many of whom have for years waged a bitter fight for existence.

Zeiss called attention to the difficulties the scientist encounters today in endeavoring to explain all phenomena on the basis of the natural sciences. It has been known for some time that typhoid epidemics are not entirely dependent on the water. Even at the risk of being decried as a mystic, Zeiss asserted that physicians should not reject astrology, without further inquiry, as having no scientific basis. Astronomical happenings should be studied, as they have a possible connection with the appearance and disappearance of epidemics.

The Relation of Physiology and Physics

Addressing the Prussian Academy of Sciences, Prof. Wilhelm Trendelenburg, of the University of Berlin, spoke on "The Relation of Physiology to Physics." This problem falls into three parts: the question of the share of physiology in the acquirement of a knowledge of the principles of physics, the question of the part played by physics in the sense perceptions, and, in studying the problem from a deeper philosophical angle, the question of the basic principles of research in both sciences and the compatibility of the "world views" based on them.

The declarations of physics concern an "objective" external world, assumed hypothetically to exist, although adequate scientific proof of its existence cannot be furnished. But all knowledge of physical objects existing outside ourselves is derived through subjective sense perceptions; hence, to that extent, physics is, essentially, subordinated to physiology. It is of interest to the physicist to obtain a measure with which to test the subjectivity of the various perceptions. In all the

more delicate inquiries the senses, such as smell, taste, touch, sense of warmth, sense of equilibrium and even hearing, must be eliminated, which leaves sight as the physical sense that is the organ of apperception *par excellence*. Of the various functions of the eye, visual acuity functions most accurately. Accordingly, the physicist always seeks to reduce the establishment of differences of shades of light (for example, in the case of light absorption by solutions or the blackening of photographic plates) to coincidence or space measurements, by the interposition of suitable apparatus. The brownian movement places a physical limitation on the sensitiveness of the various types of apparatus. The physiologic limitation is reached at the place where the points to be observed are no longer perceived to be separate and distinct. That is the case when, on the retina, the space separating the images is considerably less than 0.001 mm.; for then the stimuli no longer strike different retinal elements.

The second question concerns the physical theory of the various organs of sense. In recent years the mechanism of general nerve conductions has been studied by means of the Einthoven thread galvanometer. In observations on the acuity of smell it has been found that butterflies are capable of detecting at considerable distances the presence of almost unbelievably small concentrations of substances. Investigations on the smallest quantity of light that the human eye can detect following complete accommodation to the dark show that fifty photons suffices to produce a single light sensation. In continuous illumination, about three times as many photons per second are required. According to Noddack, a single light quantum to each of the retinal rods is sufficient for the production of light perception. Physicists have completely changed their views concerning the nature of light. How closely is physiology bound to the changing status of physical research? Would a "crisis" in physics bring about a crisis in physiology? Trendelenburg holds that, in spite of the recent upheavals in physics, one cannot speak of a crisis in that science but only of the overthrow of certain theories. That there should be a succession of theories lies in the nature of scientific research. One must take the attitude that all one can demand of a theory is that it shall be reconcilable to all ascertained facts that come within its scope. Physiology needs not to reestablish its claims to its factual acquisitions but needs only to reinterpret them.

From the lofty pinnacle of the philosopher, therefore, one views the following remarkable prospect: Physics can obtain no knowledge that is not colored, as it were, by physiology, while physiology cannot, on its own account, make any final pronouncements without consulting physics. Will the two theoretical structures support each other, or can problems arise that will effect the downfall of both? Such a menace lies in the psychophysical problem, which takes a position before all science based on observations and is independent of it. Research in the natural sciences can reveal only physical facts. The specific character of conscious experience on the "inside" of the physiologic processes is not accessible to such research.

Exhibits by the Public Library

The Badische Landesbibliothek in Karlsruhe makes a practice of organizing instructive exhibits. Just now the library is coming to the aid of the public health service. Under the heading "Literature on Health Culture" numerous manuscripts, printed works and pictures dating from the ninth to the nineteenth century have been combined in an exhibit. Of particular interest are the illustrations found in books and manuscripts produced about the year 1000 in the Reichenau cloister on Lake Constance. Then there are old prints that shed light on the development of anatomy, surgery and education of the people in hygiene and health legislation; also works of Frank and Mai, Baden's pioneers in the field of public health culture.

AUSTRALIA

(From Our Regular Correspondent)

Feb. 20, 1934.

Australasian Medical Congress

The fourth session of the Australasian Medical Congress (British Medical Association) was held at Hobart, Tasmania, the southernmost city in Australia.

CANCER RESEARCH AND TREATMENT

In 1900 the death rate of cancer in Australia was 57 per hundred thousand persons. In 1931 it was 105. For a time it was thought that this increase was fictitious, being the result of closer study and more accurate diagnosis. The time for this theory, true as it possibly was between 1900 and, say, 1910, has passed. In a scattered population such as exists in Australia, the distribution of radon is more convenient than the use of the element itself. Other advantages are that the patient under treatment by gaseous radium can leave the hospital as soon as the application is made. The danger of loss is negligible. The radium bomb has been definitely considered uneconomic; conditions requiring the bomb can be as effectively treated by high voltage roentgen therapy. Great economy is achieved, as all available energy from the radium is collected and used; the radium is never idle, many more patients can be treated, and the needles can be bent and prepared according to the specification of the surgeon. During the last seven years a sum of £373,165 has been allotted for the cancer campaign by the commonwealth and state governments and other state organizations. A total of approximately 12 Gm. of radium has been put into use. Cancer clinics have been instituted at eighteen large metropolitan hospitals as well as a number of extrametropolitan hospitals. In the four years since treatment by radium was begun on an organized basis, radium has been used in the treatment of approximately 10,000 cases of cancer. The number of cases treated by means of x-rays or surgery or by other methods in which radium has had no part is not known.

As to the success achieved, on the one hand the death rate from all forms of cancer has increased from 96 to 105 per hundred thousand in the last four years. On the other hand, although sufficient time has not elapsed to enable figures to be given in terms of the five-year series, the results of treatment are definitely improving, and the mortality statistics for 1931, based on the estimated population in the age groups for that year, showed a decline in cancer mortality in all such groups under 65 years of age.

Dr. L. J. Clendinnen of Melbourne discussed the present status of radium in the treatment of cancer. In cancer of the tongue, he said, radium treatment has been disappointing. There is an immediate response to its treatment with radium, but the growth soon recurs nearby. The use of radium has displaced surgical operation in the treatment of lip cancer, because radium is able to deal with the infiltrating border of the growth in a way that is not possible by surgical operation. In cancer of the breast, Dr. Clendinnen quoted figures of 218 patients treated in Melbourne in the last five years and showed that, of the patients in the inoperable stage treated by operation, 100 per cent had growths in adjacent areas within six months of the operation. Among the corresponding class treated with radium, the local recurrence rate was 13 per cent. He quoted these figures in support of the contention that cancer of the breast, incompletely removed, would recur more quickly than if it was treated by radium. Finally he referred to cancer of the uterus. Every patient who had sought relief from the condition, he said, had the disease in an advanced stage. He made a plea for the education of the public in the early signs and symptoms of cancer of the uterus, so that patients may

apply for treatment while there is some hope of its being successful.

The pathologic aspect of the cancer problem was discussed by Dr. J. V. Duhig of Brisbane, who said that until recently the cancer pathologist did not see much beyond the horizon of fixed tissue histology. Today no review of the pathology of cancer could be even moderately complete without a survey of the work of the experimental cytologist, pathologist and biochemist, and latterly the physicist.

Dr. E. H. Molesworth of the University of Sydney, who read a paper on the status of roentgen therapy in the treatment of cancer, said there was a strong tendency on the part of many persons to regard roentgen treatment and radium treatment as separate entities. In reality there was exactly the same difference between the two as there was between treatment by radium implanted in the tissues surrounding the growth and that by radium at a distance. Ultimately only economic considerations would determine whether a roentgen tube, radium at a few centimeters distance, or a radium bomb would be employed for a tumor in any given situation.

In a discussion on the surgical treatment of cancer, Dr. F. P. Sandes of Sydney said that cancer surgery had become a definite specialized branch of the healing art and that the time was long past when cancer should be regarded solely as a surgical disease. Cancer treatment was no longer individualistic but a matter for team work. The surgeon should be at the head of the team, but he would not be able to occupy this position unless he trained himself to fill it. In reference to work of cancer immunology carried out on animals, he said it was not too much to hope that in the near future the results obtained might be made applicable to man.

An interesting observation was made by Professor Chapman of Sydney, who investigated the cancer incidence among road workers who had been handling tar for the past thirty years. He found that cancer was less common than in corresponding age groups of the general population.

Introduction of Disease by Airplane

The development of airplane communications with Australia, traversing, as they do, the areas of endemic disease in the "East," has necessitated the provision of special quarantine arrangements in Northern Australia. With the transit time reduced to about five days from these endemic areas, a real danger has been introduced. In consultation with other countries, regulations are now being framed whereby all persons arriving in Australia from the north will be required to have been vaccinated recently against smallpox. Otherwise they will be vaccinated at Darwin. Persons suspected of carrying other dangerous diseases will be detained at the new quarantine station that is to be built at Darwin. Owing to the rarity of smallpox in Australia it is felt that the people are protected by effective vaccination. A serious outbreak in any of the thickly populated districts would have serious consequences. The England-Australia air mail will traverse some of the danger areas of the world where smallpox, cholera and yellow fever are rife. Strict measures must be taken to protect Australia from this menace. A bacteriologic and diagnostic laboratory is also being constructed at that center, which is the first port of call of airplanes arriving in Australia. Tropical disease is receiving increased attention in Australia today. Dr. R. W. Cilento has been appointed research officer in Tropical Diseases at the School of Tropical Medicine at Sydney.

Infant and Maternal Welfare in New Zealand

Another low record for infant mortality, 32.15 per thousand live births, has been established for New Zealand. This is also a world record. The birth rate was also the lowest on record. The maternal figures are not so stimulating. The total puerperal mortality rate has remained practically stationary since 1927. The mortality from the toxemias has risen slightly, that from the "accidents" of pregnancy has risen considerably, while the mortality from septic abortion has risen alarmingly. On the other hand the mortality from puerperal sepsis, excluding septic abortion, shows a most gratifying fall from 2.01 in 1927 to 0.68 in 1931. The rising returns of mortality from septic abortion are giving the New Zealand authorities great concern. Out of twenty-nine fatal cases that were officially investigated in the year 1931 twenty-six occurred in married women, which indicates that the incentives to abortion arise mainly from social and economic circumstances and not from loose living. Here is one of the most difficult problems in the whole field of maternal mortality.

During the past ten years a generous provision of hospital beds for midwifery has been made and it now amounts to one bed per thousand of the white population. During the year under review, 70 per cent of the total births took place in hospitals. It is interesting to note that there were far fewer instrumental deliveries, the forceps rate having fallen from 14.5 per cent in 1927 to 9.15 per cent in 1931. Hospital deliveries have also enabled a far wider application of the principles of surgical asepsis. It is a world-wide problem that the rising sepsis mortality from criminal abortion should counteract the improvement that is gained in the mortality from sepsis following labor. There is a trend of unofficial opinion in these parts of the world which tends toward the continental outlook on abortion.

Tetanus from Catgut

Considerable disquietude has been occasioned by the occurrence in New South Wales during the past twelve months of four cases of tetanus following surgical operations in which catgut was used. The usual method of attempted sterilization adopted is by means of red mercuric iodide and alcohol. Samples of catgut so treated have been shown bacteriologically not to be sterile and tetanus bacilli have been obtained from cultures.

Typhoid from Oysters

An epidemic of twenty-four cases of typhoid is in progress in Brisbane. Investigations by the health department showed that the patients were all supplied with oysters by one vender, who obtained them from beds that were in close proximity to the main sewer into the bay. Typhoid bacilli were isolated from samples of oysters taken from this bed.

Marriages

EUGENE JOSEPH LOVE, Petersburg, Ky., to Miss Alberta N. Sheldon of Dupont, Ind., at Lexington, Ky., Nov. 22, 1933.

JEREMIAH ROBERT JOHNSON to Miss Lois Ellis, both of Ramseur, N. C., at Chesterfield, S. C., Dec. 23, 1933.

CHESTER A. KISSINGER to Mrs. Edward Higgins, both of Milwaukee, at Woodstock, Ill., February 17.

WENDELL J. BURKETT, Pitman, N. J., to Miss Anita L. Sprigman of Woodbury, February 17.

JULIUS HOWARD STOKES, McBee, S. C., to Miss Helen Rhoad of Strawberry, Dec. 28, 1933.

CARLOS IZLAR GREEN to Miss Kittie Albergotti, both of Orangeburg, S. C., January 14.

ROY M. LANIER, Brownsville, Tenn., to Miss Mildred Jones of Memphis, February 16.

HARRY GREENSTEIN to Miss Ethel Rose Simon, both of Chicago, February 1.

ARTHUR KARL KOFF to Miss Dorothy Hess, both of Baltimore, January 17.

JAMES E. JOBES to Miss Gladys Haws, both of Indianapolis, January 25.

Deaths

Ernest Scott ● Columbus, Ohio; Ohio Medical University, Columbus, 1900; professor of pathology, Ohio State University College of Medicine since 1915, and assistant professor of veterinary pathology, 1908-1915; professor of histology, 1903-1904, and professor of pathology, 1904-1910, at his alma mater; professor of pathology, Starling-Ohio Medical College, 1908-1915; member of the American Association of Pathologists and Bacteriologists and the American Society of Clinical Pathologists; bacteriologist to the city board of health, 1904-1908; on the staff of the Columbus State Hospital and pathologist to the University Hospital; aged 58; died, March 5, at his home in Westerville, of coronary thrombosis.

William A. Frontz ● Baltimore; Johns Hopkins University School of Medicine, Baltimore, 1911; member of the American Association of Genito-Urinary Surgeons and the American Urological Association; associate professor of urology at his alma mater; served during the World War; aged 48; associate editor of the *Journal of Urology;* visiting urologist to the Sinai Hospital and assistant visiting urologist to the Johns Hopkins Hospital, where he died, March 23, of heart disease.

Maurice Packard ● New York; Columbia University College of Physicians and Surgeons, New York, 1900; on the staffs of the Gouverneur Hospital, Hospital for Joint Diseases, Broad Street Hospital and the Jewish Maternity Hospital, New York, and the Home for the Aged Infirm, Yonkers; aged 57; died, March 15, of heart disease, while en route to the Pan American Medical Congress.

William Ralph Campbell ● Major, M. C., U. S. Army, Omaha, Neb.; University of Colorado School of Medicine, Denver, 1916; served during the World War; entered the medical corps of the U. S. Army as a first lieutenant in 1918 and in 1929 was made a major; aged 44; died, March 9, in the Station Hospital, U. S. Army, Fort Leavenworth, Kansas.

Norman Smith Starr, Oklahoma City; University of Michigan Homeopathic Medical School, Ann Arbor, 1915; member of the Associated Anesthetists of the United States and Canada; served during the World War; aged 45; died, January 30, in the Veterans' Department of the Oklahoma State Hospital, Norman.

Luther Franklin Robinson, Ullin, Ill.; Hospital College of Medicine, Louisville, Ky., 1889; member of the Illinois State Medical Society; past president and secretary of the Pulaski County Medical Society; for fifteen years bank president; formerly mayor; aged 82; died, February 15, of arteriosclerosis and acute nephritis.

James Walter Reese, Cleveland; Ohio State University College of Homeopathic Medicine, Columbus, 1915; served during the World War; formerly member of the city health department; aged 41; died, March 2, in the U. S. Marine Hospital, of acute meningitis, chronic sinusitis and carcinoma of the left antrum.

Lewis Harry Adler, Jr. ● Philadelphia; University of Pennsylvania School of Medicine, Philadelphia, 1888; member of the House of Delegates of the American Medical Association in 1911; fellow of the American College of Surgeons; on the staff of the Charity Hospital; aged 69; died, March 5, of heart disease.

John Marion Wolfe, Jacksonville, Ill.; Barnes Medical College, St. Louis, 1898; member of the Illinois State Medical Society; past president of the board of education; on the staffs of Our Savior's Hospital and the Passavant Memorial Hospital; aged 62; died, February 23, of toxemia and nephritis.

William P. S. Henry, Everett, Pa.; University of Pennsylvania School of Medicine, Philadelphia, 1882; member of the Medical Society of the State of Pennsylvania; past president of the Bedford County Medical Society; served during the World War; aged 77; died, February 17, of pneumonia.

Vito Witting ● Urbana, Ill.; Royal University of Florence Faculty of Medicine and Surgery, Florence, Italy, 1926; in 1928 vice secretary to the Italian Congress of Medical Radiology; aged 30; on the staff of the Carle Memorial Hospital, where he died, February 11, of lymphatic leukemia.

Robert Joseph Shea, New York; Cornell University Medical College, New York, 1914; member of the Medical Society of the State of New York; fellow of the American College of Surgeons; on the staff of St. Elizabeth's Hospital; aged 43; died, February 15, of coronary sclerosis.

Alexander Chace Sanford, Newport, R. I.; Bellevue Hospital Medical College, New York, 1898; member of the Rhode Island Medical Society; secretary of the Newport County Medical Society; aged 59; visiting physician to the Newport Hospital, where he died, February 2.

William Farquhar Bacon ● York, Pa.; Bellevue Hospital Medical College, New York, 1882; member of the House of Delegates of the American Medical Association in 1908, and from 1916 to 1922; on the staff of the York Hospital; aged 74; died, February 15, of heart disease.

Angell Sigvart Hoiland ● Minneapolis; University of Minnesota Medical School, Minneapolis, 1910; fellow of the American College of Surgeons; aged 49; on the staff of the Lutheran Deaconess Home and Hospital, where he died, February 22, of valvular heart disease.

Thomas Francis Healey, Stamford, Conn.; Long Island College Hospital, Brooklyn, 1908; member of the Connecticut State Medical Society; served during the World War; aged 51; died suddenly, March 16, in the Stamford Hospital, of perforated duodenal ulcer and peritonitis.

Henry Seaton Hutchison, Toronto, Ont., Canada; University of Toronto Faculty of Medicine, 1900; assistant professor of medicine at his alma mater; physician in charge of the outpatient department of the Toronto General Hospital; aged 54; died, January 6.

James E. Mason, Stettler, Alta., Canada; Western University Faculty of Medicine, London, Ont., 1914; fellow of the American College of Surgeons; ship surgeon on the S. S. *Niagara;* aged 48; died, in January, on board ship on the Pacific Ocean.

Elmer Ellsworth Vorhies, Cambridge, Ohio; Starling Medical College, Columbus, 1893; member of the Ohio State Medical Association; formerly county coroner and state senator; aged 68; died, February 11, in the Swan Hospital, of heart disease.

Charles Tracie Henderson, Gouverneur, N. Y.; Syracuse (N. Y.) University College of Medicine, 1911; member of the Medical Society of the State of New York; on the staff of the Stephen B. Van Duzee Hospital; aged 54; died, February 7.

Henry A. Brierly, Peculiar, Mo.; University Medical College of Kansas City, Mo., 1895; member of the Missouri State Medical Association; aged 65; died, March 1, in the Wesley Hospital, Kansas City, Mo., of coronary thrombosis.

Herbert Halsey Hurd ● Chippewa Falls, Wis.; Rush Medical College, Chicago, 1878; past president of the Chippewa County Medical Society; aged 81; died, March 9, in St. Joseph's Hospital, as the result of a fractured hip received in a fall.

La Vern I. Rogers ● Galesburg, Mich.; University of Michigan Medical School, Ann Arbor, 1907; aged 51; on the staffs of the Borgess Hospital and the Bronson Hospital, Kalamazoo, where he died, February 12, of pneumonia.

Albert E. Hoff ● North Bend, Neb.; Central Medical College of St. Joseph, Mo., 1898; fellow of the American College of Physicians; past president of the Dodge County Medical Society; aged 63; died, January 27, of heart disease.

Alfred Jesse Stewart, Ontario, Calif.; Hahnemann Medical College and Hospital, Chicago, 1896; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1906; aged 65; died, January 13.

John Wesley Robinson, Grand Rapids, Mich.; Illinois Medical College, Chicago, 1900; on the staff of the Michigan Soldiers' Home Hospital; aged 62; died, March 7, in the Butterworth Hospital, of cerebral hemorrhage.

Manly Eugene Siler, Mercer, Tenn.; Memphis Hospital Medical College, 1907; member of the Tennessee State Medical Association; for many years president of the school board; aged 51; died, February 12, of heart disease.

Henry Wade, Starksboro, Vt.; University of Vermont College of Medicine, Burlington, 1883; member of the Vermont State Medical Society; health officer; aged 81; died, January 2, of injuries received in an automobile accident.

Carlton Victor Wilder, Atlantic, Iowa; Hahnemann Medical College and Hospital, Chicago, 1882; member of the Iowa State Medical Society; on the staff of the Atlantic Hospital; aged 82; died, February 13, of heart disease.

Algernon Winston Walden, Owingsville, Ky.; College of Physicians and Surgeons, Baltimore, 1883; county health officer; at one time member of the state board of health; aged 77; died, February 28, of cerebral hemorrhage.

Le Roy Boyd, Birmingham, Ala.; Medical College of Alabama, Mobile, 1887; member of the Medical Association of the State of Alabama; aged 70; died, February 21, of angina pectoris and arteriosclerosis.

Campbell Ford, San Francisco; University of California Medical Department, 1891; member of the California Medical Association; aged 69; died, February 11, of an incised wound of the throat, presumably self inflicted.

Edward Evan Sargent ● Le Roy, Ill.; Miami Medical College, Cincinnati, 1893; for twelve years president of the school board; aged 65; died, February 20, in the Brokaw Hospital, Normal, of agranulocytosis.

Arthur E. Walker ● Anthony, Kan.; Medical College of Indiana, Indianapolis, 1892; past president and secretary of the Harper County Medical Society; aged 73; died, February 5, of cerebral hemorrhage.

Osmond Nason Hoyt, Long Beach, Calif.; Hahnemann Medical College and Hospital, Chicago, 1879; formerly superintendent of the state board of health of South Dakota; aged 90; died, Dec. 30, 1933.

George L. Morgenthau ● Chicago; Dartmouth Medical School, Hanover, N. H., 1888; for many years on the staff of the Michael Reese Hospital; aged 71; died, March 21, of colitis and morphine poisoning.

George Dill Rowe, East Providence, R. I.; Medical School of Maine, Portland, 1889; member of the Maine Medical Association; aged 67; died, March 3, when he was unable to escape from a burning hotel.

Octavus P. Large ● Philadelphia; Medico-Chirurgical College of Philadelphia, 1898; aged 65; died, March 14, in the Temple University Hospital, of cellulitis of the neck and septicemia.

Oscar O. Blakeslee, Conneaut, Ohio; College of Physicians and Surgeons, Baltimore, 1882; city health officer; aged 80; died, February 28, in the Brown Memorial Hospital, of pneumonia.

Birt B. Reeder, Clarksville, Fla.; Georgia College of Eclectic Medicine and Surgery, Atlanta, 1910; aged 54; died, March 2, in a hospital at Dothan, Ala., of carcinoma of the stomach.

Joseph Lemuel Campbell, Bristol, Tenn.; Chattanooga Medical College, 1902; member of the Tennessee State Medical Association; aged 58; died, February 17, of myocardial insufficiency.

Alexander Abraham Aron, Philadelphia; University of Pennsylvania School of Medicine, Philadelphia, 1906; aged 50; died, March 5, in the Mount Sinai Hospital, of cardiovascular disease.

Bertha Caroline Downing, Kennebunk, Maine; Woman's Medical College of Pennsylvania, Philadelphia, 1896; aged 72; died, Nov. 21, 1933, of chronic nephritis and intestinal hemorrhage.

George Munson Vandegrift, New York; University of the City of New York Medical Department, 1879; aged 80; died suddenly, February 10, in Snow Hill, Md., of heart disease.

Edward Sutherland Winbigler ● Alexis, Ill.; Rush Medical College, Chicago, 1893; for many years member of the school board; aged 66; died, February 12, of hepatic cirrhosis.

James Mitchell Hartley, Hollywood, Fla.; Atlanta Medical College, 1915; member of the Florida Medical Association; aged 45; died, February 19, of a self inflicted bullet wound.

Albert Asa Cannaday ● Roanoke, Va.; University of the City of New York Medical Department, 1888; aged 70; died, February 22, in the Shenandoah Hospital, of Ludwig's angina.

Thomas Emmett McDermott, Minneapolis; Chicago Medical College, 1883; aged 77; died, February 20, in St. Barnabas Hospital, of uremia and carcinoma of the prostate.

Mat Marshall McRee, Dallas, Texas; Vanderbilt University School of Medicine, Nashville, Tenn., 1901; aged 57; was found dead, February 26, of a self-inflicted bullet wound.

George M. Stillman, Argyle, N. Y.; Albany Medical College, 1885; formerly county coroner; aged 75; died, February 24, of arteriosclerosis and chronic myocarditis.

Frederick Kellogg Hollister, East Hampton, N. Y.; New York Homeopathic Medical College and Hospital, 1895; aged 64; died, February 4, of carcinoma of the larynx.

James Willard Bazell ● Winslow, Ariz.; University of Louisville (Ky.) School of Medicine, 1909; formerly health officer of Winslow; aged 52; died, Dec. 22, 1933.

Lamont B. Smith, Youngstown, Ohio; Cleveland Homeopathic Medical College, 1898; aged 56; died, February 12, in St. Elizabeth's Hospital, of cardiorenal disease.

James Rutherford Bingham ● New York; Trinity Medical College, Toronto, Ont., Canada, 1893; aged 71; died, March 9, in the Doctors Hospital, of pneumonia.

Thomas Sheldon Taylor, Schellsburg, Pa.; University of Louisville (Ky.) School of Medicine, 1907; aged 47; died, February 10, in Miami, Fla., of acute nephritis.

Samuel Addison Roberts, Salem, Ind.; University of Louisville (Ky.) School of Medicine, 1882; county health officer; aged 73; died, March 2, of nephritis.

S. Hilton Buker, Killbuck, Ohio; Medical College of Ohio, Cincinnati, 1887; member of the Ohio State Medical Association; aged 69; died, March 8, of nephritis.

Minnie Dell Baker, Nashville, Mich.; Hahnemann Medical College and Hospital, Chicago, 1891; aged 75; died, in February, at Grand Rapids, of myocarditis.

Oscar Lee Wilson, Rushville, Neb.; Medical College of Indiana, Indianapolis, 1879; aged 76; died, January 20, of chronic myocarditis and arteriosclerosis.

Parker Fiske Wesley, Haviland, Kan.; Hospital College of Medicine, Louisville, Ky., 1905; aged 50; died, February 19, in a hospital at Pratt, of acute nephritis.

George W. Richardson, Dundee, Mich.; University of Buffalo School of Medicine, 1878; also a pharmacist; aged 81; died, March 7, of cerebral hemorrhage.

Henry Marcellus Johns, Waco, Texas; University of Tennessee Medical Department, Nashville, 1895; aged 70; died, January 31, of cerebral hemorrhage.

Jeremiah R. Sturtevant, Theresa, N. Y.; Albany Medical College, 1872; aged 86; died, January 19, of chronic myocarditis and concussion of the brain.

Robert Lincoln Watkins ● New York; University of the City of New York Medical Department, 1887; aged 70; died, February 28, of lobar pneumonia.

Frederick Graham Brien, Elphinstone, Manit., Canada; University of Manitoba Faculty of Medicine, Halifax, 1894; aged 71; died, Dec. 30, 1933.

Basil Dennis Spalding, Richmond, Va.; University of Maryland School of Medicine, Baltimore, 1891; aged 70; died, February 17, of myocarditis.

John Boasman Rone, Oklahoma City; University of Louisville (Ky.) School of Medicine, 1893; aged 71; died suddenly, February 8, of myocarditis.

William Lockwood West, New Matamoras, Ohio; Jefferson Medical College of Philadelphia, 1874; aged 83; died, in February, of pneumonia.

Edward Payson Waid, Whitmore Lake, Mich.; Chicago Medical College, 1887; aged 71; was found dead, February 16, of valvular heart disease.

Frank M. Wright, Indianapolis; Indiana Eclectic Medical College, Indianapolis, 1889; aged 75; died, February 14, of pulmonary tuberculosis.

Lewis F. Hammonds, Dunnville, Ky.; University of Louisville School of Medicine, 1897; aged 65; died, February 21, of cerebral hemorrhage.

William Clark Watson ● Bridgeport, Conn.; Long Island College Hospital, Brooklyn, 1897; aged 60; died, January 22, of heart disease.

Austin Roy Harman, Lubec, Maine; Jefferson Medical College of Philadelphia, 1896; aged 61; died, January 22, of angina pectoris.

William Arnold Christian ● Chicago; Cincinnati College of Medicine and Surgery, 1899; aged 62; died, February 4, of brain tumor.

Joseph L. Smith, Hoagland, Ind.; Eclectic Medical Institute, Cincinnati, 1878; aged 82; died, February 22, of chronic myocarditis.

Emil C. Schoene, Milwaukee; Chicago Physio-Medical College, 1895; aged 70; died suddenly, February 13, of coronary sclerosis.

John Albert Christilaw, Winnipeg, Manit., Canada; Manitoba Medical College, Winnipeg, 1914; aged 61; died, January 23.

Cyrus Henry Cutter, Aurora, Ill.; Rush Medical College, Chicago, 1881; aged 76; died, March 4, of coronary sclerosis.

Henry Rosenblith, Chicago; Illinois Medical College, Chicago, 1900; aged 63; died, February 14, of coronary thrombosis.

Daniel Webster Shier, Weston, Ont., Canada; Trinity Medical College, Toronto, 1895; aged 65; died, January 8.

Aaron G. Rogers ● Parker, Ind. (licensed, Indiana, 1897); aged 84; died, February 9, of carcinoma of the prostate.

Correspondence

TREATMENT OF AMEBIASIS

To the Editor:—There is a communication in THE JOURNAL, Dec. 2, 1933, pages 1819-1820, signed by Dr. J. C. Geiger and others, with respect to the various drugs used in the treatment of human amebiasis due to infestation with Endamoeba histolytica. In this, reference is made on page 1820, column 2, paragraphs 2 and 4, to the use of "bismuth subcarbonate in massive doses" in the treatment of this infestation, and a paper by the late Dr. W. E. Deeks and myself in the *American Journal of Tropical Medicine* (3:97 [March] 1925) is mentioned. Kindly permit me to correct an error here.

It is bismuth subnitrate, not the subcarbonate, that was first used in this manner by Dr. Deeks. I do not have at hand this copy of the *American Journal of Tropical Medicine*, and my supply of reprints has been exhausted. I am referring, however, to the original paper, which was entitled "The Etiology, Symptomatology and Treatment of Intestinal Amebiasis," by Dr. Deeks and myself. This appeared in the Proceedings of the International Conference on Health Problems in Tropical America, published by the United Fruit Company in 1924, pages 271-308.

I make this correction because Dr. Deeks and myself at first and myself later tried bismuth subcarbonate in massive doses and found that the results were not as good as when the subnitrate was given. The dose is a heaping teaspoonful well mixed in milk or water from three to five times a day.

I have used this treatment since it was first advocated by Deeks and Shaw in the *Medical Record*, Nov. 13, 1909.

In acute dysentery its use should be supplemented by emetine when this can be given under experienced supervision. It has been known for many years and reported that emetine is a dangerous drug and that its toxic effects cannot be predicted. These may come on after the first dose or later at any time during the course of treatment. It is particularly dangerous in patients with any form of myocardial degeneration or weakness. At present I would not advocate the use of bismuth subnitrate in the acute fulminating types of amebic dysentery, as I believe that valuable time might be lost. These cases are in my opinion best treated by a wide open cecostomy and thorough irrigations through the cecostomy and through the rectum as well. This method was used by Dr. A. B. Herrick, when he was chief of the surgical clinic in the old Ancon Hospital, during the construction days of the Panama Canal, before Rogers had reintroduced emetine, and it was found to be very effective in the acute fulminating types and also in the chronic types that did not yield to other treatment.

In the milder types of amebic dysentery, however, and especially in the chronic forms of infestation without diarrhea and dysentery, I have found bismuth subnitrate very useful indeed. It should be given over a period of two or three months and I have never seen any harm result, except in two cases in which the bismuth was contaminated with antimony, and these were long ago.

Several theories have been advanced as to why bismuth subnitrate is efficacious, and these were discussed by Dr. Deeks and myself in the paper referred to. However, at this time I believe it is efficacious solely as an astringent. Very likely it also cleans out the amebas living in the lumen of the bowel and prevents these from entering the tissues.

In a paper entitled "Human Amoebiasis Due to Infection with Entamoeba Histolytica" (*Ann. Trop. Med. & Parasitol.*, August 1928) I stated that I believe if the ulcers and other pathologic lesions of the large intestine can be caused to heal, the amebas in the tissues will disappear, and I am still of this belief; otherwise there would be no permanent cures.

I should not like to be understood as claiming that bismuth subnitrate is a true specific and always cures the infestation, since I have used other drugs frequently in conjunction with it; but for me it is a sheet anchor.

In addition to the articles you mention that may be consulted with respect to amebic dysentery in the footnote to your review of this subject in THE JOURNAL, Nov. 18, 1933, page 1639, permit me to suggest "The Amoebae Living in Man," by Clifford Dobell, published in 1919 by William Wood & Co., New York, and the chapter on the "Entamoebae of Man," in "Protozoology," by C. M. Wenyon, volume I, page 84, also published in 1926 by William Wood & Co. Any one interested in the study of human amebiasis will find these authoritative and instructive.

In several communications received from friends at home they have mentioned the difficulty they are encountering in using the wet fixation and Heidenhain's iron hematoxylin method of staining. I had much trouble years ago in learning to use this method correctly. In the *Annals of Tropical Medicine and Parasitology* 8:133-320 (July) 1914, is an article of mine entitled "A Study of the Entamoebae of Man in the Panama Canal Zone." In this article I put down all the troubles which I encountered and endeavored to describe in detail the various methods of wet fixation and staining which were in use at that time and are still useful today. Dr. R. B. H. Gradwohl described wet fixation and staining in THE JOURNAL, Jan. 6, 1934, page 65, which covers most of the essential points. I myself should advise the use of slides and not of cover glasses, as the latter are difficult and very troublesome to handle.

I have found that fixation in a modified Schaudinn's fluid, consisting of two parts of physiologic solution of sodium chloride saturated with corrosive mercuric chloride and one part of 96 per cent or absolute ethyl alcohol, plus the addition of from 2.5 to 5 per cent of glacial acetic acid, has given me better results than the aqueous solution saturated with corrosive mercuric chloride, without the acetic acid. The weaker acetic acid solution is better for the delicate trophozoites in acute and subacute dysentery, and the stronger solution gives better fixation for cysts. I believe that from twenty to sixty minutes is too long a time for fixation of thin stool smears, since most authorities find that from five to ten minutes is ample. I prefer to fix at room temperature, as the heated fixing solutions produce artefacts, as has been pointed out by Leland Cleveland.

In step 6 of his article, Dr. Gradwohl does not mention that the preparations should be thoroughly rinsed after mordanting. It is very important that this be done, two separate containers holding at least 1 liter of water each being used. If the preparations are not thoroughly rinsed, an excess of the mordant is carried over into the hematoxylin solution, making decolorization difficult, and the amebas are likely to appear a dirty yellow with indistinct nuclei, instead of showing a clear gray cytoplasm with sharply defined and clear cut black or deep purple nuclei.

Also in step 6, Dr. Gradwohl has omitted to state that the hematoxylin solution should be diluted one half with distilled water before using. The 1 per cent stock solution is too strong. It is not necessary, though advisable, to allow the solution to ripen for four weeks before using. If it is thoroughly aerated by allowing a current of air to pass through it over night, it will be ready for use in the morning. The diluted solution should be filtered, after use, into a clean bottle. Later, this filtered diluted solution should be used with an equal part of the original stock solution, diluted one half, then filtered again into the second bottle, and so on until the original stock solution is used up, when there will be two bottles of stain. These can be used undiluted repeatedly, and they improve with use until

the hematoxylin is finally precipitated. This can be told by adding a few drops of the stain to a test tube half full of tap water. If the resulting color is yellow or green, the stain is no longer useful; if the color is blue or violet, the stain is still good. Only a good quality of distilled water should be used for diluting the stock solution; tap water or alkaline water will precipitate the hematoxylin or, rather, the hematin, which is the active staining principle. The staining solutions should be kept in brown glass bottles, away from the light.

Free living amebas can be obtained easily in the zoological laboratories of most of our universities at home. If these are used for practice, the necessary skill and judgment can be obtained by those unfamiliar with the method more readily than by using stool smears in the beginning. Wet fixation and staining is a tiresome method, but I do not know of any other that will give such accurate results in distinguishing the five species of amebas found in the stools.

William M. James, M.D., Panama, R. P.

DENTAL CARIES

To the Editor:—I have read with interest the editorial on dental caries published in The Journal, February 17, and I would like to submit the following comment:

There have appeared recently in several periodicals (including *Science* **78**:419 [Nov.] 1933) articles by Bunting and his associates in the University of Michigan which claim emphatically, and with an air of finality, that the etiology of dental caries has been fully established by them, and that Lactobacillus acidophilus is the active causative agent.

Such an assertion, if based on adequate scientific evidence, would in the last analysis imply three things: (1) that caries is caused by a specific organism; (2) that the organism is a lactobacillus, and (3) that the lactobacillus is unequivocally L. acidophilus.

1. The bacterial etiologic concept still lacks general support. This is revealed by a general review of papers appearing in dental journals, and by unpublished statements of investigators of dental pathology. So-called proof of bacterial etiologic relationship appears still to be far from complete.

2. Researches during the past six or seven years have impressed on me the numerical importance of high acid-producing streptococci in caries and noncaries mouths, a compared with lactobacilli. By following the quantitative plating method devised and recommended by Rodriguez (*J. Am. Dental A.* **17**:1711 [Sept.] 1930), my associates and I demonstrated the occurrence of millions of high acid-producing bacteria per cubic centimeter of saliva, but these proved, on close observation, to be streptococci essentially, instead of lactobacilli, as featured by Rodriguez and later by Mrs. Hadley. If bacterial acids do play an important rôle in dental caries, is it not plausible that streptococci should be even stronger contributing factors in caries production than lactobacilli?

3. In spite of certain isolated claims to the contrary, the lactobacilli of the mouth and tooth cavities are of definite "oral" type and differ in several important respects from the "intestinal" types, including L. acidophilus. Some of these fundamental differences were stressed by me (*Yale J. Biol. & Med.* **4**:485 [March] 1932). Morishita (*J. Bact.* **18**:181 [Sept.] 1929) recognized the aciduric organisms of the mouth and intestine as being different. Researches of the past two years have strongly confirmed my belief in the diversity of the two general types.

Some writers claim to have shown that mouth lactobacilli may be dissociated into rough forms which resemble L. acidophilus of the intestine. Their observations were incomplete and not convincing. More recently, Weinstein, Anderson and Rettger (*J. Dental Research*, August 1933) failed in attempts to derive one type from another. Dissociation was effected to a certain point but could not be carried further.

I do not wish to detract from the work of those whose claims are so strongly at variance with my own. I take this occasion, however to protest against the high powered claims made and reiterated again and again by these investigators. In the present limited state of knowledge regarding the etiolgy of caries, conservatism is the safer course. Little can be gained, for example, by referring to the mouth lactobacilli as L. acidophilus.

Leo F. Rettger, Ph.D., New Haven, Conn.
Professor of Bacteriology, Yale
University School of Medicine.

LOCAL ANESTHETICS IN ARTICULAR PAIN

To the Editor.—The recent reply of Dr. J. C. Weisman (The Journal, March 3, p. 714) to the criticism (January 13, p. 148) of the use of local anesthetics in articular pain (Paris letter, Nov. 4, 1933, p. 1492) so supported my experience that I desire to add my own observations. I have not used such treatment in acute conditions.

In chronic painful articular conditions, two recent cases have convinced me of the efficacy of local anesthesia in certain cases. I would feel hesitant in using it in unquestioned infection or in polyarthritis. But occasionally a case appears in which there are no definite demonstrable infective foci and drug therapy appears to be ineffectual. These persons are disabled, are never free from pain, and have usually made the rounds of doctors and have had a session with the chiropractors.

H. M., a man, aged 43, seen in bed, for nearly one year, after a fall on the ice, had severe pain in and about the right hip joint. The pain was worse at night and was lancinating. His only relief was through occasional opiates. He was financially unable to have medical care. He walked only with effort and pain. One cubic centimeter of 1 per cent quinine and urea hydrochloride was given deep into the muscles about the right hip joint. Severe pain followed for about twelve hours, followed by nearly complete relief. A second treatment was given four days later. The nocturnal pain ceased. He was able to walk and today, four months later, he has only a slight limp.

T. S., a man, aged 40, a C W A employee, referred to me by the preceding patient, had been troubled by a painful stiff right hip, with darting pain down the back of the leg along the course of the sciatic nerve. This had continued for one year. He had taken some drugs but had been given many chiropractic adjustments with no relief. Physical examination showed definite infected (carious) teeth, but otherwise nothing. He was advised to have the teeth cared for. In the meantime he was given 0.5 cc. of 2 per cent solution of procaine hydrochloride into the muscles about the right sciatic notch. Twenty-four hours later he reported relief. At intervals of three to five days he was given two more injections of 0.5 cc. of 1 per cent quinine and urea hydrochloride. After the second treatment he was able to dance. For a week diathermy treatments and massage were given, and in the third week he was discharged free from all pain. At the end of two months he is still a grateful patient.

Naturally, I know that statistics cannot be considered accurate when based on two cases; but I believe that local anesthetics, administered with aseptic care in the region of a persistently painful joint, should be given consideration.

R. E. Logan, M.D., Galena, Ill.

A CASE OF EXTRA-OCULAR MUSCULAR PARESIS TREATED WITH GLYCINE

To the Editor:—A man, aged 32, first came to one of us (H. N. B.), Aug. 27, 1928, complaining of a recent diplopia. Paresis was present of all the muscles of the left eye supplied by the internal and external branches of the third cranial nerve. There was only a slight ptosis of the upper lid. The patient has been under systemic treatment ever since that time. He had an extremely sluggish patella reflex. Blood examination was negative. The Wassermann reaction of the blood and spinal fluid was negative. He was given several doses of neoarsphenamine and a mercury compound and potassium iodide internally. Examination of the paranasal sinuses gave negative results. He had some infected teeth, which were removed. The possibility

of multiple sclerosis was considered and a diagnosis was made by an English neurologist of myasthenia gravis, though there was a distinct inequality of the pupils.

The history of this case has been one of continued improvement and regression. The vertical diplopia, which worried him most, would improve and so would the ptosis. The extraocular muscles of the right eye would then become affected as the left eye had been.

On the patient's return from England last summer, he was placed on ephedrine at the suggestion of the neurologist in London, and there was some improvement noticed immediately. Then (after consultation with H. H. B.) glycine was given in the hope that we would obtain benefit from its administration in this unusual case. At the end of several weeks the condition improved so much that it was no longer necessary to cover one eye with an opaque lens, for the diplopia was no longer a source of discomfit to the patient. Since in this case there had been periods of improvement under the former treatment combined with rest, we were at first inclined not to be too sanguine, but the patient is firmly convinced that this period of improvement has lasted longer and that he has approached a more normal state than at any time since the beginning of the trouble. The patient is an extremely intelligent man and has given his condition a thorough analysis and expresses himself to be delighted with the improvement made.

H. H. BEARD, PH.D.,
H. N. BLUM, M.D.,
Departments of Biochemistry and Ophthalmology,
Louisiana State University Medical Center,
New Orleans.

IDIOSYNCRASY TO SALYRGAN

To the Editor:—I have read with interest Dr. Carter Smith's report on the use of salyrgan in one patient over a period of three years (THE JOURNAL, February 17, p. 532). He states that only one instance of idiosyncrasy to salyrgan has been reported in the literature, that by Andrews in the *Lancet*, July 18, 1931. I wish to point out that Dr. Bongiorno and I reported a case of sudden death due to salyrgan in a nephrotic child, aged 4, in the *Canadian Medical Journal* (**25**:73 [July] 1931). The injection preceding the fatal one caused a chill, fever, a morbilliform rash, anorexia and malaise. Good diuresis was obtained, whereas previous injections failed to provoke a satisfactory response. A week later the sixth and fatal dose was given, causing sudden death, which was anaphylactic in nature

I. J. WOLF, M.D., Paterson, N. J.

THE RELATION OF THE USE OF ALCOHOL AND TOBACCO TO CORONARY OCCLUSION

To the Editor:—In connection with the article of Drs. White and Sharber on the relation of alcohol and tobacco to angina pectoris (THE JOURNAL, March 3, p. 655) a brief report on the effect of these substances on coronary occlusion is, I think, of interest.

Of 150 patients with coronary occlusion seen in private practice, 52 per cent were total abstainers, 34 per cent occasionally used alcohol and 14 per cent were habitual drinkers. Of a group of 150 patients with the same age and sex ratios who did not have coronary occlusion, 48.6 per cent were total abstainers, 40.6 per cent occasionally used alcohol and 10.6 per cent habitually used alcohol. There was therefore no apparent relation between the use of alcohol and coronary occlusion, with the exception that one or two patients in the series developed occlusion during a period of exhaustion following a prolonged debauch. Of the same group of patients with coronary occlusion, 34 per cent were nonsmokers, 36.6 per cent moderate smokers (not more than twenty cigarets or three cigars or pipes a day) and 30 per cent were excessive smokers. Of the control group, 34 per cent were nonsmokers, 33.3 per cent moderate smokers and 32.6 per cent excessive smokers.

The number of cases analyzed is, of course, too small to warrant sweeping conclusions. Yet the figures suggest that, as in angina pectoris, so in coronary occlusion the use of alcohol and tobacco is of little if any significance.

GEORGE BLUMER, M.D.,
New Haven, Conn.

Queries and Minor Notes

ANONYMOUS COMMUNICATIONS and queries on postal cards will not be noticed. Every letter must contain the writer's name and address, but these will be omitted, on request.

LEUKOCYTE COUNT IN APPENDICITIS

To the Editor:—A patient having the symptoms and signs of acute appendicitis has the usual leukocytosis, with more than 90 per cent polymorphonuclear leukocytes. Is there any danger in doing the operation with the polymorphonuclear count 90 per cent or above? One surgeon of my acquaintance will not operate on a patient showing 90 per cent or more. Is this good surgical judgment? What change occurs, if any, in the blood count of the same patient as described when the appendix ruptures? Please give other signs of a ruptured appendix. Kindly omit name.

M.D., Oklahoma.

ANSWER.—A percentage of polymorphonuclear leukocytes in appendicitis of over 90 indicates pus or gangrene, usually with a peritonitis. Occasionally there may be pus under tension. In general, the high percentage of polymorphonuclears indicates a severe infection or a massive toxic absorption, while a high total count indicates a high resistance. No matter how low the total count, a high percentage of polymorphonuclears indicates a very severe toxemia.

Following perforation there may be a preliminary rise of the total count, but when toxic absorption becomes excessive there is a drop, which may extend well below normal. However, the percentage of polymorphonuclears rises rapidly to over 90.

The differential count is the most important laboratory finding to differentiate between an improved and a more serious condition.

The general condition, including pulse rate, fever, blood pressure and local symptoms, will be the deciding factor in determining the diagnosis and the probability or length of time since perforation. Since the total count is usually high early after perforation with a high polymorphonuclear percentage, the presence of a falling total count or a rising percentage of polymorphonuclears is indicative of a progressive peritonitis and a grave prognosis.

The Schilling method of differential count is of value in prognosis, since the increase of early or immature forms of neutrophilic leukocytes is of serious significance regardless of the total count.

With a perforation and spreading peritonitis, the outcome is usually fatal unless the peritonitis is localized to the region of the appendix or the source is removed in the first twenty-four hours.

In most cases the peritonitis remains localized and becomes walled off. Because of this fact, most physicians do not wish to operate with a peritonitis unless the patient is seen shortly after perforation. However, unless there is evidence of the peritonitis becoming walled off by localized symptoms or a mass, it is quite likely that if the peritonitis continues to spread the patient will die unless a leaking perforated appendix is removed.

With a localized peritonitis, as evidenced by a mass or very localized symptoms suggesting periappendicular abscess, operation should be delayed. Most of these masses will subside and after two or three months the appendix should be removed.

If the toxemia increases with evidence of a local abscess, it should be drained, preferably after a week's time. The drainage should be made without opening the general peritoneal cavity either through a muscle splitting incision, or, in a pelvic abscess, through the rectum.

A polymorphonuclear increase of over 90 is not a contraindication to operate. It indicates the critical time for use of

the best surgical judgment as to the necessity for immediate operation, following a careful clinical examination. Only the immediate removal of a leaking perforated appendix with a spreading peritonitis can prevent a fatal outcome, while breaking up adhesions in a walled off peritonitis or perforated appendicitis should not be done by operation in the early stages.

ADMINISTRATION OF IRON—SODIUM CACODYLATE—COD LIVER OIL

To the Editor:—Will you kindly send me information concerning the following questions: What are the relative merits of iron given orally and hypodermically? What is the relative quantity absorbed by these two methods? What is the value of sodium cacodylate injections as compared with an iron injection such as Fraisse's Feruginous ampoules? Do you consider cod liver of tonic value for adults?

PAUL GEARY, M.D., Plainfield, N. J.

ANSWER.—Hypodermic administration avoids local action on the alimentary tract; but this can be avoided also by proper administration of suitable iron salts by mouth; e. g., insoluble preparations such as ferrous carbonate or poorly ionized iron compounds such as iron and ammonium citrate. When iron is injected all of it is absorbed, but most of it so rapidly eliminated (chiefly by the large intestine) that the amount which remains in the system is probably no larger than the quantity which remains when the iron is absorbed from the alimentary tract. Arsenic, whether administered in the form of cacodylate or otherwise, acts in a different manner from iron in that the former tends to increase the number of red blood corpuscles, the latter the amount of hemoglobin, when administered in suitable cases. Cod liver oil is of tonic value only when there is a deficiency of vitamin A or D or of easily assimilable fat in the diet.

LUPUS ERYTHEMATOSUS AND SYPHILIS

To the Editor:—Kindly inform me as to the prognosis and the latest treatment of lupus erythematosus in a young married woman who contracted syphilis about one and half years ago and who was under neoarsphenamine and bismuth treatment for that length of time. Do you think there is a possibility of any relationship between the treatment of syphilis and the skin condition? If so, is it advisable to continue with the antisyphilitic treatment? Please omit name.

M.D., New York.

ANSWER.—The prognosis in lupus erythematosus depends entirely on the type of the disease. It is poor in the acute disseminate variety with grave constitutional symptoms and fever. In the subacute disseminate variety the outlook is fair. In the ordinary chronic discoid type the prognosis is good, although the course of the disease may be capricious and recurrences are not infrequent. The latest method of treatment is by intravenous injection of gold sodium thiosulphate, beginning cautiously with doses of from 5 to 10 mg. and reaching a maximum of from 50 to 100 mg. once weekly. Serious reactions have been reported from gold therapy, but in properly selected cases the results are excellent. When there is intolerance to gold, bismuth compounds may be tried intramuscularly. Local treatment will depend entirely on the severity of the inflammatory symptoms. At times, light freezing with carbon dioxide snow may be beneficial.

There is no relationship between the treatment for syphilis and the development of lupus erythematosus. Antisyphilitic treatment should be continued only if the serologic reaction is still positive or if clinical evidence of syphilis is still present.

POSTOPERATIVE GAS PAINS

To the Editor:—What is the most recent theory as to the etiology of postoperative gas pains and what is the present concept as to the prevention and treatment? After a recent appendectomy the patient complained of gas pains for eight days, in spite of enemas, rectal tubes and solution of pituitary. Some surgeons advocate castor oil on the second or third day after operation. Is this considered good practice? Please omit name and address.

M.D., Iowa.

ANSWER.—There is little after-effect on the movements of the gastro-intestinal tract due to etherization, section of the abdominal wall or exposure to the air with cooling.

The paralyzing effect on the bowel is less under local than under general anesthesia. Spinal anesthesia paralyzes the inhibitors and permits overactivity of the propulsive peristalsis.

The loss of propulsive peristalsis is constant after intestinal operations, while the rhythmic pendular movements may continue to function. A general reflex inhibition may be produced reflexly through the splanchnics by stimulation of the intestine or of any sensory surface at operation.

Following any intestinal operation a localized loss of motor function occurs, especially of the propulsive peristalsis, varying with the extent of trauma to some extent. The pylorus may contract reflexly and delay evacuation as a protective mechanism to the intestine.

The distention of the intestine may to a large extent be prevented by maintaining tonus and the rhythmic contractions with morphine sulphate, although propulsive persistalsis may be but slightly affected. The protective action of morphine has recently been advocated in general peritonitis to prevent overdistention with complete paralysis of the wall.

The recent use of a concentrated sodium chloride solution intravenously and as an enema has been highly satisfactory for postoperative distention. An enema of 150 cc. of a 10 per cent solution of sodium chloride gives better results than the usual treatment advocated for gas pains or distention.

Castor oil both before and after operation has been abandoned by most surgeons. Catharsis will tend to spread a localized peritonitis and is dangerous in appendicitis.

Large enemas may produce a similar bad effect and should be given for distention or gas pains only after that possibility has been considered.

Fecal impaction or colon stasis perhaps antedating operation may necessitate the flushing type of enema but rarely catharsis.

USE OF X-RAYS IN ACNE VULGARIS

To the Editor:—I should like to have your experience in the use of x-ray tubes as a therapeutic agent in the treatment of acne vulgaris. Do you know where a technician could go to take a course in roentgen therapy? I will appreciate any information that you can give as to the advisability of the use of x-rays. J. T. GRAY, M.D., Stillwater, Okla.

ANSWER.—Permanent cures can be obtained in selected cases of acne vulgaris to the extent of 87 per cent with roentgen treatment plus general medical attention. From eight to sixteen weekly treatments are usually required. It is the most certain way to obtain a permanent cure in three or four months. The treatment is not without danger and should be given only by a physician who is well trained in x-ray work and also who knows a great deal about acne vulgaris. Courses in roentgen therapy are given in many places. Courses in so-called superficial roentgen therapy are given at the New York Post-Graduate Medical School. Courses may also be obtained at the Mayo Clinic, at the New York University and Bellevue Hospital Medical College and many other places. The indications and contraindications for the roentgen treatment of acne vulgaris are contained in chapter 28, page 431, of MacKee's book on X-rays and Radium in the Treatment of Diseases of the Skin, Philadelphia, Lea and Febiger, 1927.

DIFFERENTIAL DIAGNOSIS OF EDEMA

To the Editor:—A woman, aged 40, has an edematous condition involving the whole body. It does not pit on pressure. It is worse at certain times than at others. It is worse in the early morning but on exercise tends to disappear to some extent. The face seems to be more affected than other parts of the body. The heart and kidneys are normal. Allergy does not seem to play any part. What other conditions would you consider as an etiologic factor? Please omit name.

M.D., Arkansas.

ANSWER.—This question does not supply information relative to the duration of the condition and other physical signs apart from the edema. It must be remembered that any edema of long standing tends to lose its pitting characteristic.

A general, nonpitting edema without cardiovascular or renal disease would suggest the following conditions:

1. Myxedema, which occurs most commonly between 30 and 50 years of age and more commonly in women than in men. The puffiness occurs most noticeably about the face and eyes, with characteristic swelling of the ankles and wrists. It is associated with a masklike expression, with mental and physical sluggishness, and with an extremely low basal metabolic rate. It may appear spontaneously or may follow thyroidectomy. The response to thyroid therapy is usually satisfactory.

2. Chronic heredotrophedema (Milroy's disease), which comes on early in life and usually affects only the lower extremities. In cases in which the upper part of the body has been involved the swelling has never been so great as that observed in the lower extremities.

3. Beriberi, a deficiency disease. Here the edema pits on pressure, unless of long standing, and it is associated with other ailments, particularly a peripheral neuritis.

4. "Nutritional edema," thought to be due to a lack of protein in the diet together with an overabundance of fluid and salt. This edema usually pits on pressure and the dietetic errors should aid in the diagnosis.

From the information given, myxedema seems most likely.

ACETIC ACID IN RINGWORM

To the Editor:—In Queries and Minor Notes in THE JOURNAL, Dec. 2, 1933, I noticed Dr. Rittenhouse's inquiry regarding a local application that would be effective in ringworm of hairy regions. The answering discussion mentions iodine and croton oil but does not name a simple remedy that I have found to be successful. Three dermatologic textbooks that I have examined also do not list this application.

Several years ago I noticed a barber making an application to a ringworm on a patron's face and inquired what he was using. The solution was 18 per cent acetic acid and the barber told me that one or two applications invariably cured the condition and that he also used it for barber's itch (sycosis). Being quite sure that 18 per cent acetic acid would at least do no harm, I began using this application for ringworm, both on hairy regions and otherwise, and have had constantly good results. Any tineal infection may be thus treated. I have used it in a few mild cases of epidermophytosis (athlete's foot) with benefit. The only objection is the burning caused by the application, which is, however, of short duration. The application of acetic acid is not repeated sooner than three days. The ordinary ringworm subsides after one or two treatments. An infected ringworm of the scalp was treated six or seven times before it became inactive. Usually ammoniated mercury ointment is prescribed to be used after the application of the acetic acid.

I do not know who may have originated this treatment of ringworm or whether it is in common use, but it has proved a satisfactory treatment of a common and usually stubborn condition.

A. L. NIELSON, M.D., Harlan, Iowa.

ANSWER.—Acetic acid has been used as a remedy for ringworm for a long time. Kaposi (Hautkrankheiten, Vienna and Leipzig, Urban and Schwarzenberg, 1880, p. 740) lists it as one of many remedies for ringworm of the scalp. H. R. Crocker (Diseases of the Skin, ed. 2, Philadelphia, P. Blakiston's Son & Co., 1893, p. 865) recommends it for the treatment of tinea circinata, to be painted on the patch after it has been thoroughly cleansed with soap and water. Of modern writers O. S. Ormsby (Diseases of the Skin, ed. 2, Philadelphia, Lea & Febiger, 1921, p. 892) mentions acetic acid as an adjuvant to other remedies, using it with or just before the other parasiticide. On the next page he lists glacial acetic acid as one of the strong remedies for ringworm of the scalp.

ANTIQUITY OF THE USE OF OPIUM

To the Editor:—What preparation of the poppy was first used in the practice of medicine, and when? What drug was used for the relief of pain during the first fifteen years of the eighteenth century?

C. C. HOWARD, M.D., Glasgow, Ky.

ANSWER.—Opium, the dried juice of the unripe poppy capsules, was no doubt known in remote antiquity, though infusions of poppy capsules and the pulp of unripe poppy seeds were probably used still earlier. The papyrus of Ebers (1552 B. C.) mentioned "spenn" seeds in the preparation of a "remedy to prevent the excessive crying of children." Hippocrates (460 B. C.) described the properties of the juice of the white poppy. Its employment at that time was chiefly in the form of highly complex mixtures: such as the "mithridatium" of Damocrates or the theriaca of Andromachus. There can be no doubt that it was opium that was chiefly used for the relief of pain in the early part of the eighteenth century. In the later part of the seventeenth century, Thomas Sydenham had introduced its alcoholic tincture, made from opium and saffron with wine (Sydenham's laudanum), as the greatest of all remedies; and paregoric originated with Dr. Le Mort, professor of chemistry at the University of Leyden between 1702 and 1718. It was also at this time that Dover, the inventor of Dover's powder, practiced. A proprietary preparation known as "black drops," which was a vinegar of opium, was also extensively used at that time.

RINGWORM OF TOENAIL

To the Editor:—One of my patients has a ringworm of both great toes following athlete's foot. This infection does not appear to affect the surface of the nail but has undermined the lateral edges for about one third of the nail's width. Please suggest treatment. Please omit name.

M.D., Michigan.

ANSWER.—Ringworm of the nails is one of the most stubborn forms of fungous infection. Great patience and perseverance in treatment are required to cure it by nonsurgical methods; but this is possible in most cases. Tincture of iodine, best applied in the case described with a medicine dropper, the solution being allowed to run under the nail, is one of the best remedies. After daily use for a time irritation is apt to occur, when a soothing ointment, as 10 per cent boric acid in petrolatum, may be applied for a day or two, then Whitfield's ointment, 6 per cent salicylic acid and 12 per cent benzoic acid in ointment of rose water, may be used daily for several weeks. Another course of the iodine solution should then be given. No preparation of mercury should be used while the effect of the iodine remains, for fear of a dermatitis. It is often necessary to change remedies several times before a cure can be achieved. Many other remedies are recommended, among the best of them an alcoholic solution of thymol, 1 per cent or stronger, or salicylic acid 10 per cent or corrosive mercuric chloride, 1:500, in alcohol.

One-fourth erythema dose of unfiltered x-rays, once a week for a maximum of eight weeks, or a stronger dosage of filtered x-rays if the nail plate alone is exposed, are sometimes successful when other measures fail. The rest of the finger should be protected by lead, and no irritating local application should be used for from two weeks before until two weeks after the treatment. After the effect of the rays has passed off, one or more of the remedies mentioned should be used for, if not wholly eradicated, the disease will recur.

Avulsion of the nail is seldom necessary but may be done if all else fails. It is best done under general anesthesia and followed by an iodine ointment, about 5 per cent, until the nail grows again, which requires about five months.

FINGER SUCKING BY CHILDREN

To the Editor:—A boy, aged 4½, has nursed the two middle fingers of each hand, chiefly the right, since birth only when sleepy or asleep. He has developed normally in every way and had an attack of enteritis for four weeks when 13 months of age. Intervention to cure the habit was not begun early enough, and over the past year taping the fingers and splints to the elbows have been tried without success. The only local change noticed is a slightly loose condition of the two upper middle teeth. He exhibits a nervous tendency and recently has begun to bite his nails. I am in doubt as to whether to urge cure of the habit or recommend no treatment at all. Would the methods to use for such a cure tend to aggravate his nervousness? Your recommendation mentioning methods will be appreciated.

H. QUILLIAN JONES, M.D., Fort Myers, Fla.

ANSWER.—Finger sucking or thumb sucking is of common occurrence in infancy and young childhood. As stated in the query, it is most likely to occur when the child is sleepy or asleep, or when he is nervous, fatigued or sick. The habit may persist from infancy into childhood. Most of these children recover from the habit spontaneously, though sometimes it continues for a considerable period.

The condition is sometimes difficult to treat, though if the child is manifestly nervous it is well to manage the general condition by rest, quiet, and the avoidance of overstimulation and fatigue. If too much is made of the condition, the habit may become worse and may continue in spite of attempts to forbid it, or by promises of reward or threats of punishment. The application of ill tasting substances to the fingers gives only temporary results. A rubber nipple or pacifier may at times be used as a temporary substitute for the thumbs or fingers, though even this method usually fails. Globular aluminum mitts to cover the hands or thumbs prevent the introduction of the fingers into the mouth. In many cases the habit is stopped when the child grows older, and too strenuous treatment may tend to increase general nervousness and induce other bad habits.

ALOPECIA IN CHILDREN

To the Editor:—Family history, Wassermann reaction, and so on, being negative, what could one think of in a girl, aged 4 years, otherwise healthy, with a growing depression over the right parietal bone and progressive clean baldness?

CLARENCE B. FOSTER, M.D., Greensboro, Vt.

ANSWER.—Alopecia may occur from one to six months after an acute fever. The hair begins to fall out, though this seldom leads to baldness. In mycosis fungoides, diabetes mellitus, myxedema or the cachexia of tuberculosis the hair may fall out and the condition may remain permanent. Alopecia is sometimes seen after the administration of thallium acetate or boric acid. It is observed after toxic doses of mercury, antipyrine or arsphenamine. Congenital or acquired syphilis may cause alopecia.

In alopecia areata the hair is suddenly lost. The baldness occurs in sharply defined areas without signs of inflammation. The patches tend to spread peripherally. They are frequently multiple. Alopecia areata rarely occurs under 5 years of age. The affected scalp may be thinner than normal and the area is frequently depressed below the level of the surrounding skin.

Alopecia areata must be distinguished from ringworm, although the former is rapid in onset and spreads diffusely, and the bald areas are smooth and show no fungi, scales, vesicles or crust. In ringworm the fungus may be demonstrated and the extension of the bald area is slower.

Impetigo, erysipelas or other violent inflammatory diseases of the scalp may cause temporary bald areas, but the disease causing the loss of hair is readily observed.

PROPHYLACTIC VACCINATION AGAINST RABIES IN DOGS

To the Editor:—I have been unable to obtain satisfactory information as to whether the antirabies serum administered to dogs for the purpose of preventing rabies is considered effective in the prevention of this disease. Could you give me any information concerning this?

WILLIAM S. CRAWFORD, M.D., Tulsa, Okla.

ANSWER.—There is no antirabies serum for the prevention of rabies. Prophylactic injection of dogs against rabies is done with so-called vaccines of the fixed virus. There are two such vaccines available; namely, the phenol-treated and the chloroform-treated. In both these vaccines the virus is either dead or rendered so avirulent that it does not produce rabies in rabbits on subdural injection. At present the experiments with the chloroform vaccine are encouraging, but no data are available as to its efficacy under field conditions (Schoening, H. W.: Prophylactic Vaccination of Dogs Against Rabies, *J. Am. Vet. A.* **78**:703 [May] 1931). The maximum duration of immunity after vaccination is thought to be one year.

CALCULATION OF LOSS OF VISION

To the Editor:—I was interested in an article in a recent issue of *Hygeia* by James E. Lebensohn, entitled "Mysteries of Vision." I have been puzzled several times to know the percentage loss of vision in compensation cases and would like to know more in detail the mathematics for the authors' calculations of various losses of vision. As I understand it, the insurance companies consider a vision of 20/200 or less a total loss of vision as far as work is concerned. A vision of 20/30 is considered a 10 per cent loss of vision.

HOWARD L. MITCHELL, M.D., Lexington, Va.

ANSWER.—On the basis of personal clinical investigations, A. C. Snell (THE JOURNAL, Oct. 31, 1925, p. 1367) found that total incapacity lay between a visual acuity of 20/200 and 2/200, determined by the nature of the employment, the age of the person, the duration of subnormal vision, and the will to work. Though most states have ruled that 20/200 is industrial blindness, mathematically this visual acuity represents a general visual efficiency of 20 per cent. Test charts can be procured from Bausch and Lomb, Rochester, N. Y., that, alongside the distance notations, have the A. M. A. ratings of visual efficiency. The full table with a consideration of the various factors involved in the determination of visual acuity has been presented by J. E. Lebensohn in the *Archives of Ophthalmology* **10**:103 [July] 1933). For details of the method of calculation, the article entitled "Percentage Evaluation of Macular Vision," by A. C. Snell and S. Sterling (*Arch. Ophth.* **54**:443 [Sept.] 1925), should be consulted.

ANTISTREPTOCOCCUS SERUM IN ERYSIPELAS

To the Editor:—What is the present status of antistreptococcus serum in septicemia and in erysipelas?

MERVIN T. SUDLER, M.D., Lawrence, Kan.

ANSWER.—The use of antistreptococcus serum in septicemia rests on an empirical basis. There is no evidence available to show that such treatment is specifically successful. The use of antistreptococcus serum in erysipelas is based on the demonstration that the streptococcus of erysipelas produces a specific toxin against which a specific antitoxin can be produced by immunization of horses with the toxin. In other words, in the case of erysipelas there is available a specific antitoxic serum which, according to many reports, gives good results in early cases. However, not all reports of the results with the serum are favorable.

ELECTROCUTION WITHOUT MARKS ON SKIN

To the Editor:—Is there sufficient experimental or clinical data to determine whether or not one can become electrocuted by coming in contact with electric light wires without having evidence of receiving burns on the skin?

ROSS TRIGG, M.D., Fort Worth, Texas.

ANSWER.—Current markings of the skin are not always present in cases of electrocution caused by currents of low tension (110 volts). Several cases have been reported in which most careful search failed to detect external evidences of electrocution (Meixner, K.: *Wien. klin. Wchnschr.* **35**:619 [July 13] 1922. Fürth: *München. med. Wchnschr.* **64**:926, 1917. Jellinek, S.: *Wien. klin. Wchnschr.* **36**:157 [March 1] 1923. Spuren: Kunde der Elektrizität, Vienna, 1927). In some instances the current markings are easily overlooked, especially if they are located in regions of the body covered by hair or are on the hands of laborers with a thickened scaly skin. Examination with the aid of a hand lens may help to detect these insignificant changes. On the tips of the fingers, finger prints may help to locate the current marks, since in this region the normal linear markings are obscured.

TOXIN-ANTITOXIN AND TOXOID

To the Editor:—I noticed in Queries and Minor Notes in THE JOURNAL, Nov. 18, 1933, page 1663, an inquiry concerning immunity. I have had diphtheria four or five times. I received three courses of toxin-antitoxin in different years. The Schick test is still positive but the reaction is less severe each time. I took two injections of toxoid and the Schick test was negative.

JOHN G. WILSON, M.D., Norristown, Pa.

ANSWER.—The treatment of diphtheria with antitoxin tends to reduce the active immunity, so that it is quite possible for a person thus treated to have more than one attack of diphtheria. The prompt neutralization of the toxin by the antitoxin reduces the reactions of the body against the toxin. When the passive immunity due to the antitoxin subsides, the person in question may become susceptible again to diphtheria toxin. The fact that the Schick test was positive after the injection of toxin-antitoxin means that adequate active immunity had not been established at any time. On the other hand, the two injections of toxoid appear to have established sufficient active immunity to make the Schick test negative.

PARENT'S BLOOD INJECTION AS PROPHYLACTIC IN MEASLES

To the Editor:—Please tell me whether an injection of blood from a parent who has had measles into a child will prevent measles. If so, what amount? Kindly omit name.

M.D., Georgia.

ANSWER.—Yes, the injection of such blood will prevent measles if it is injected in the incubation period. At least 4 or 5 cc. should be injected intramuscularly, and this quantity would better be doubled or quadrupled in older children and when the injection is made late in the incubation period.

SYPHILITIC PERIOSTITIS AND TABES

To the Editor:—Kindly advise as to the treatment of syphilitic chronic periostitis of both legs as evidenced by x-rays. The blood Wassermann reaction is negative; the spinal Wassermann was not taken. Infection occurred twenty years ago, and a few injections of neoarsphenamine were given. There are severe night pains at intervals, varicose veins, marked wasting of the calf muscles, and absent knee jerks. The pupils react sluggishly. The patient shows low blood pressure and loss of weight. Would such a case react to bismuth injections and iodides by mouth?

M.D., Pennsylvania.

ANSWER.—The absent knee jerk, sluggish pupils, nocturnal pains and wasting of the calf muscles suggest tabes or at least neurosyphilis. A spinal puncture should be done and a more complete neurologic examination. Chronic periostitis of the legs due to late syphilis should improve with injections of bismuth compounds, and iodides by mouth. These should alternate with courses of mercurial inunctions and small doses of one of the arsphenamines.

NO INCOMPATIBILITY IN MIXTURE OF CACODYLATE, SALICYLATE AND METHENAMINE

To the Editor:—Would you please let me know what results when sodium salicylate is mixed with hexamethylenetetramine (methenamine) and also what is formed when sodium cacodylate, sodium salicylate and hexamethylenetetramine are all mixed together? Kindly omit name.

M.D., Alabama.

ANSWER.—Mixtures of these substances were made and solutions of these mixtures in water were prepared and both allowed to stand forty-eight hours. Neither the dry mixture nor the solutions showed the slightest evidence of change.

PSITTACOSIS

To the Editor:—The question has come up as to possible hazards to public health in handling birds other than parrots and parrakeets. I wonder whether you can tell me if any other species, particularly canary birds, are sometimes subject to psittacosis or any other disease which is transmitted to man.

M. J. LAKE, M.D., New York

ANSWER.—The investigations of K. F. Meyer and his associates in San Francisco have shown conclusively that other birds than parrots and parrakeets may suffer from psittacosis. Meyer and Eddie (Spontaneous Psittacosis Infections of the Canary and Butterfly Finch, *Proc. Soc. Exper. Biol. & Med.* **30**:481 [Jan.] 1933) report the occurrence of psittacosis in a man and his wife who came in contact with canary birds having

the disease, to which they are highly susceptible. Canary birds may harbor paratyphoid-like organisms and consequently become a possible source of food poisoning. The birds also may harbor coccal organisms in the respiratory tract which may be pathogenic for human beings.

APPENDICITIS WITH WORMS

To the Editor:—Recently I examined an appendix that contained Oxyuris vermicularis in large numbers. How frequently does this parasite produce an appendical disturbance simulating an acute appendicitis? Please omit name.

M.D., Illinois.

ANSWER.—Such observation is quite common, and it is agreed that the worms may cause appendicitis. They may produce appendical colic; they may irritate the mucosa sufficiently to cause catarrhal inflammation, and even hemorrhagic areas; and they may penetrate into the walls of the appendix, carrying infection with them. The frequency with which they actually produce symptoms simulating appendicitis is still quite as much *sub judice* as the more hotly debated question regarding the importance of fecaliths. It is, however, not great.

ACTION OF GLYCERIN HYPODERMICALLY

To the Editor:—I request that you supply me with information on the action of chemically pure glycerin on the tissues if used hypodermically. What are its irritant qualities when used in this way in full strength or undiluted or in any dilution with water? It is understood, of course, that the preparation would be sterilized.

H. T. CUMING, M.D., Pace, Miss.

ANSWER.—Glycerin is an irritant when injected in full strength or in any but great dilution. It also causes laking of the blood, owing, it is believed, to an osmotic effect on the red blood corpuscles during their passage through the area in which it has been deposited.

INSULIN IN DEMENTIA PRAECOX

To the Editor:—Kindly give me the latest treatment of dementia praecox with insulin. A Viennese physician, Dr. Zackel, is supposed to have obtained superb results. I am interested, as I have a relative who has dementia praecox. The treatment requires putting the patient into insulin shock. Could you give me detailed information regarding this treatment?

M.D., New York.

ANSWER.—We are not acquainted with the work of Dr. Zackel. His name does not appear anywhere in the last ten volumes of the *Quarterly Cumulative Index Medicus*, which lists all medical publications of any importance. Insulin is not mentioned as a remedy for dementia praecox in the comprehensive paper on endocrine treatment of the psychoses by Hoskins and Sleeper in the *American Journal of the Medical Sciences* (184:158 [Aug.] 1932). On the other hand, insulin is frequently used in the treatment of all forms of psychosis with malnutrition due to unwillingness of the patient to take food.

HOLZKNECHT'S SPACE

To the Editor:—What is Holzknecht's space with respect to the left lateral border of the heart on a roentgenogram? Kindly omit name.

M.D., Pennsylvania.

ANSWER.—Holzknecht's space refers to the middle lung field in the roentgen screen or film image of the chest in oblique projection, when the rays pass from the left posteriorly to the right anteriorly. In this projection there are three clear lung fields: the right, the left and the middle (Holzknecht's). This space is also referred to as the retrocardiac or the prevertebral space, bounded anteriorly and to the left by the posterior border of the heart, and to the right and posteriorly by the vertebral column.

CRIMSON ANILINE CRYSTALS OR ROSANILINE HYDROCHLORIDE

To the Editor:—In Queries and Minor Notes in THE JOURNAL, Oct. 7, 1933, page 1173, under "Preparations of Cadavers for Dissection in Tropical Countries," you mention "crimson aniline crystals" for coloring the injection mass. I am unable to procure this chemical. It is not even mentioned in any of the books that are at my disposal here. Will you be kind enough to let me know another name or chemical formula under which it can be obtained, possibly the source of its manufacture? Please omit name.

M.D., Colorado.

ANSWER.—Crimson aniline, aniline red, basic fuchsin and magenta are trade names for the same thing; namely, a preparation of rosaniline hydrochloride. The dye may be obtained from any of the dealers in dyestuffs.

TRAUMA AND MYOCARDITIS

To the Editor:—An obese man of 69 was struck by an automobile, Sept. 17, 1933, and sustained some contusions and shock. He is bringing suit against an automobile insurance company to recover damages on the ground that the injury produced an acute exacerbation of a chronic myocarditis and permanent and total disability as a result. Is it at all likely that the previous heart condition could be made worse by the accident? Please omit name.

M.D., Minnesota.

ANSWER.—The accident itself obviously could not have altered myocardial conditions. It does occasionally happen that preexisting conditions are first called to the patient's attention after such an accident, when they are discovered by the attending physician. It is possible that the enforced rest and altered circulatory conditions might accentuate some condition already present, but it does not seem possible that this could be more than temporary. It does not seem at all probable that permanent and total disability could result.

PROTECTION IN ROENTGENOGRAPHY

To the Editor:—I am subjected to x-rays in my work to the extent of half an hour of fluoroscopic work approximately five times a week. I should like an opinion if you feel that this might be sufficient to cause any feeling of fatigue or produce any secondary anemia. I do not use any lead gloves, goggles or protective apron. Please omit name and address.

M.D., Michigan.

ANSWER.—Half an hour of fluoroscopic work approximately five times a week may cause fatigue but not secondary anemia. It is imprudent not to use protective measures, such as apron and gloves.

OPERATIVE TREATMENT FOR SACRO-ILIAC SPRAIN

To the Editor:—What is the present status of the operative treatment for sacro-iliac sprain?

MERVIN T. SUDLER, M.D., Lawrence, Kan.

ANSWER.—The operative treatment of chronic recurring sacro-iliac pain is surgical fusion and is generally accepted. However, the surgeon should exclude such possibilities as arthritis of the lumbar spine, cord tumor and spondylolisthesis before resorting to this operation.

CHANCROIDS

To the Editor:—In Queries and Minor Notes in THE JOURNAL, January 20, page 231, Dr. H. B. Taylor of Anking, China, asks for "the latest and best treatment for chancroids." I have my own method, used since 1907, and I believe it is much better than any treatment you mention in your reply. It consists of ordinary cleansing and the application of one of the following solutions: (1) 25 per cent thymol iodide in ether; (2) 25 per cent iodoform in ether. Solution 2 is the stronger and more effective, but the odor of the iodoform often precludes its use in society, in which case I use solution 1, which is slower and not as good as solution 2. The ether vehicle is the successful keynote to its effectiveness, as it carries the drugs quickly into the deeper tissues and ulcerated hidden recesses before the ether evaporates, thus leaving the drug in direct concentrated contact all over the involved areas. The slight pain at the time of application lasts only a few seconds. It gives instant relief. As it quickly flows into all involved areas it is seldom necessary with its use to perform deep slits or circumcisions if syphilis is not also present. Both solutions are simple, quick, sure, always available, cleansing, soothing and easy of application, and save many patients from the necessity of going to bed. They are also far superior to Menciére's solution even in buboes. The first day or two a few drops should be poured on the involved areas three or four times and as healing progresses and pain decreases the number of applications can be reduced to once or twice a day, as indicated. The patient will soon tell of the relief obtained and will ask for it in preference to all other forms of treatment. I perfected these solutions while on duty on the Asiatic Station in 1907 and have used them ever since. Once tried, all other methods of treatment for this painful and distressing disease will be discarded.

PAUL RANDOLPH STALNAKER, M.D., Houston, Texas,
Captain, Medical Corps, U. S. Navy, Retired.

"LIVER GROWN"

To the Editor:—In Queries and Minor Notes in THE JOURNAL, Oct. 28, 1933, p. 1414, there was an inquiry as to the term "liver grown" as used in the Pennsylvania Dutch counties of Pennsylvania, and in the issue of Feb. 24, 1934, a reply by Dr. Yoder. The term as I have heard it used refers to enlarged abdomens, particularly those that occur in rachitic children. A physician with whom I worked a number of years ago, when rachitis was seen in more advanced stages than it is seen now and whose early years had been spent in the Dutch counties, often referred to the "pot bellied" child as "liver grown." His explanation of the term was that no one among the natives realized the actual etiology of the condition but, knowing that the liver was the largest abdominal organ, believed that the "pot belly" was the result of liver enlargement. He further stated that individuals with abdominal neoplasms and at times dropsical persons were referred to in the same manner. In corroboration of his explanation, I have since heard the natives of these counties refer to enlarged abdomens as "liver grown."

ARTHUR D. KURTZ, M.D., Philadelphia.

Council on Medical Education and Hospitals

COMING EXAMINATIONS

American Board of Dermatology and Syphilology: *Written.* Examinations will be held in various cities, April 30. *Oral.* Cleveland, June 11-12. Sec., Dr. C. Guy Lane, 416 Marlboro St., Boston.

American Board of Obstetrics and Gynecology: *Oral* (all candidates), Cleveland, June 12. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh.

American Board of Ophthalmology: Cleveland, June 11 and Butte, Mont., July 16. *Application must be filed at least 60 days prior to date of examination.* Sec., Dr. William H. Wilder, 122 S. Michigan Blvd., Chicago.

American Board of Otolaryngology: Cleveland, June 11. Sec., Dr. W. P. Wherry, 1500 Medical Arts Bldg., Omaha.

Arkansas: *Basic Science.* Little Rock, May 7. Sec., Mr. Louis E. Gebauer, 701 Main St., Little Rock. *Regular.* Little Rock, May 14-15. Sec., Dr. A. S. Buchanan, Prescott. *Homeopathic.* Little Rock, May 8. Sec., Dr. Allison A. Pringle, Eureka Springs. *Eclectic.* Little Rock, May 8. Sec., Dr. L. L. Marshall, 820 W. 14th St., Little Rock.

California: *Reciprocity.* San Francisco, May 16. Sec., Dr. Charles B. Pinkham, 420 State Office Bldg., Sacramento.

Illinois: Chicago, April 10-12. Supt. of Regis., Dept. of Regis. and Edu., Mr. Eugene R. Schwartz, Springfield.

Minnesota: Minneapolis, April 17-19. Sec., Dr. E. J. Engberg, 350 St. Peter St., St. Paul.

National Board of Medical Examiners: The examinations in Parts I and II will be held at centers in the United States where there are five or more candidates, May 7-9 (limited to a few centers); June 25-27, and Sept. 12-14. Ex. Sec., Mr. Everett S. Elwood, 225 S. 15th St., Philadelphia.

Nebraska: *Basic Science.* Omaha, May 1-2. *Application must be filed at least 15 days prior to date of examination.* Dir., Bureau of Examining Boards, Mrs. Clark Perkins, State House, Lincoln.

Nevada: Carson City, May 7. Sec., Dr. Edward E. Hamer, Carson City.

New Mexico: Santa Fe, April 9-10. Sec., Dr. P. G. Cornish, Jr., 221 W. Central Ave., Albuquerque.

Missouri October Report

Dr. E. T. McGaugh, state health commissioner, reports the written examination held in Kansas City, Oct. 17-19, 1933. The examination covered 14 subjects and included 81 questions. An average of 75 per cent was required to pass. Seven candidates were examined, all of whom passed. Nine physicians were licensed by reciprocity and 2 by endorsement. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
University of Kansas School of Medicine		(1933)	85.2
St. Louis University School of Medicine		(1933)	87.1
Creighton University School of Medicine		(1930)	89
University of Nebraska College of Medicine		(1933)	87.8
University of Pennsylvania School of Medicine		(1932)	88.5
National University of Ireland		(1921)	89
University of Edinburgh Faculty of Medicine		(1923)	86.1

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
University of Arkansas School of Medicine		(1932)	Arkansas
University of Illinois College of Medicine		(1930)	Texas
University of Kansas School of Medicine		(1933)	Kansas
University of Louisville Medical Department		(1896)	Kansas
University of Maryland School of Medicine		(1908)	Maryland
University of Tennessee College of Medicine		(1930), (1931)	Tennessee
Baylor University College of Medicine		(1932)	Texas
McGill University Faculty of Medicine		(1922)	Michigan

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
Washington University School of Medicine		(1929)	N. B. M. Ex.
Jefferson Medical College of Philadelphia		(1932)	N. B. M. Ex.

Michigan Endorsement Report

Dr. J. Earl McIntyre, secretary, Michigan State Board of Registration in Medicine, reports 48 physicians licensed by endorsement during 1933. The following schools were represented:

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
College of Med. Evangelists	(1915), (1929), (1932), (1933)		California
University of Colorado School of Medicine		(1931)	Colorado
Howard University College of Medicine		(1930)	Maryland
Loyola University School of Medicine		(1927), (1928)	Illinois
Northwestern University Medical School	(1928), (1932), (1933)	(1912)	Nebraska, Illinois
Rush Medical College	(1928), (1932), (1933)	(1926)	Ohio, Illinois
University of Illinois College of Medicine	(1933)	(1926)	S. Dakota, Illinois
Indiana University School of Medicine		(1929), (1931)	Indiana
State University of Iowa College of Medicine		(1931), (1932)	Iowa
Johns Hopkins University School of Medicine		(1919)	Maryland
College of Physicians and Surgeons, Boston		(1926)	Mass.
Univ. of Michigan Dept. of Medicine and Surgery		(1898)	N. Dakota
University of Minnesota Medical School	(1928), (1930)	(1927)	Alaska, Minnesota
Barnes Medical College, Missouri		(1904)	Missouri
St. Louis University School of Medicine		(1927)	Missouri
Creighton University School of Medicine		(1931)	Penna.
University of Nebraska College of Medicine		(1924)	Nebraska
University of Buffalo School of Medicine		(1932)	New York
Ohio State University College of Medicine		(1917)	Ohio
Toledo Medical College		(1913)	Ohio
University of Cincinnati College of Medicine		(1920)	Ohio
Western Reserve University School of Medicine		(1930)	Ohio
Temple University School of Medicine		(1931)	New Jersey
University of Pennsylvania Department of Medicine		(1908)	Penna.
University of Pittsburgh School of Medicine		(1929)	Penna.
Meharry Medical College		(1932)	Tennessee
University of Texas School of Medicine		(1926)	Texas
Marquette University School of Medicine		(1932), (1933)	Wisconsin
University of Wisconsin Medical School	(1931)	(1929)	Oklahoma, Illinois
University of Toronto Faculty of Medicine		(1925)	Maryland
McGill University Faculty of Medicine		(1925)	Maine

Maryland December Report

Dr. Henry M. Fitzhugh, secretary, Board of Medical Examiners of Maryland, reports the written examination held in Baltimore, Dec. 12-15, 1933. The examination covered 9 subjects and included 90 questions. An average of 75 per cent was required to pass. Thirty-nine candidates were examined, all of whom passed. Four physicians were licensed by reciprocity. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
George Washington University School of Medicine	(1933) 87.1, 91.8	(1930)	83.3,
Georgetown University School of Medicine	(1932) 83, 85.3, 85.7, 86.9, 88.6, 89.3, 92.9, (1933) 80.8, 82.4, 85.8, 86.6, 86.7, 88.1, 88.6, 88.6, 88.6, 89.2, 89.9, 90.3, 92.6	(1931)	88.2,
Howard University College of Medicine	(1932) 79.6	(1931)	83.3,
Emory University School of Medicine		(1929)	84.6
Tulane University of Louisiana School of Medicine		(1933)	86.7
Johns Hopkins University School of Medicine	85.8, 91.4	(1933)	77.3,
University of Maryland School of Medicine and College of Physicians and Surgeons		(1933)	89.8
Washington University School of Medicine		(1928)	90.7
University of Nebraska College of Medicine		(1933)	89.3
University of Rochester School of Medicine		(1932)	80.9
Duke University School of Medicine		(1933)	86.7, 87
Medical College of Virginia		(1933)	85.1
Medizinische Fakultät der Friedrich-Wilhelms-Universität, Berlin		(1932)	88.6

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
Fort Wayne College of Medicine, Indiana		(1892)	Ohio
Indiana University School of Medicine		(1931)	Indiana
University of Pennsylvania School of Medicine		(1932)	Penna.
Medical College of the State of South Carolina		(1931)	S. Carolina

Mississippi Reciprocity and Endorsement Report

Dr. Felix J. Underwood, secretary, Mississippi State Board of Health, reports 7 physicians licensed by reciprocity and 1 by endorsement at a meeting held in Jackson, Dec. 7, 1933. The following schools were represented:

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
Tulane Univ. of Louisiana School of Med.		(1930), (1932)	Louisiana
Columbia Univ. College of Physicians and Surgeons		(1932)	Louisiana
Memphis Hospital Medical College		(1889)	Tennessee
University of Tennessee College of Medicine		(1929, 2)	Tennessee
Vanderbilt University School of Medicine		(1930)	Tennessee

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
University of Virginia Department of Medicine		(1926)	N. B. M. Ex.

Tennessee December Examination

Dr. H. W. Qualls, secretary, Tennessee State Board of Medical Examiners, reports the written examination held in Memphis, Dec. 21-22, 1933. The examination covered 8 subjects. An average of 75 per cent was required to pass. Eleven candidates were examined, all of whom passed. The following school was represented:

School	PASSED	Year Grad.
University of Tennessee College of Medicine		(1933, 11)

Two physicians were licensed by endorsement during December. The following schools were represented:

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
George Washington University School of Medicine		(1928)	Mississippi
Louisville Medical College		(1903)	Mississippi

Book Notices

Principles and Practice of Physical Therapy. Edited by Harry E. Mock, B.S., M.D., D.Sc., Chairman of the Editorial Board, Associate Professor of Surgery, Northwestern University Medical School, Ralph Pemberton, M.S., M.D., F.A.C.P., Professor of Medicine in the Graduate School of the University of Pennsylvania, and John S. Coulter, M.D., D.T.M., F.A.C.S., Assistant Professor of Physical Therapy at Northwestern University Medical School. In three volumes. Fabrikoid. Price, $35 per set. Various pagination. Hagerstown: W. F. Prior Company, Inc., 1934.

It is significant that a topic which was on the borderland of scientific medicine in a previous generation should have advanced so greatly in the past twenty years as to require the development of a three-volume system for the presentation of the available data and the scientific considerations involved in its practice. A survey of the available books in this field indicates the need for a work of this type, since present-day physical therapy represents for the most part a combination of empiricisms of the past with the scientific dictums of the present. Because of the unsettled state of our knowledge in this field the American Medical Association established the Council on Physical Therapy. The present system, edited by three members of the Council, represents some of the order that has been brought into the field by the Council's work.

Volume I, entitled "Medicine," discusses physical therapy in various medical fields but is concerned also with such basic subjects as physiology of muscular action, posture, the history of physical therapy, the bases and the uses of exercise, heat and massage in medical conditions, the use of hyperpyrexia, and many similar topics. There are twenty-four chapters in the volume, all of them exhaustive, authoritative and practical.

The second volume is concerned more particularly with surgery. Here there are twenty-five chapters discussing fractures, traumatic injuries to the joints, nerve injuries, plastic surgery, obstetric paralysis, cancer of the skin, gynecologic conditions, and other topics.

The final volume, on the technic of physical therapy, is no doubt the volume most needed by general practitioners as well as by specialists and technicians in this field. It is essentially a book of directions. However, the instructions are supplemented in each instance by a statement as to the basis for the technic employed, the indications and the dangers.

The books are well printed in the form already tested as to its popularity by the systems of surgery and of medicine issued by the same publisher. The loose-leaf system offers an opportunity for keeping abreast of the times in a work in which progress is so rapid that only the loose-leaf system would seem to offer any guarantee against obsoleteness at an early date.

Handbuch der Biochemie des Menschen und der Tiere. Herausgegeben von Prof. Dr. phil. et med. Carl Oppenheimer. Ergänzungswerk. Band I: (Ergänzung zu Band I-III des Hauptwerkes.) Halbband I: Die Baustoffe der tierischen Substanz. Halbband II: Biochemie der Zelle. Second edition. Paper. Price, 74 marks. Pp. 1154, with 40 illustrations. Jena: Gustav Fischer, 1933.

These supplements cover the literature up to 1932 in three parts: first, on building stones in animal tissues, second, on biochemistry of the cell and, third, on specific binding power and antibodies. These sections are subdivided on nearly the same basis as the original work. Several new subdivisions were necessary and several new contributors have been added or substituted. The first part is presented as follows: the inorganic constituents of the animal body, by Hans Aaron, Karl Klinke and K. Scharrer; four sections on simple nitrogen-free combinations up to five-carbon compounds, carbohydrates and derivatives, benzene derivatives of nitrogen-free cyclic compounds, and amino sugars, by Heinz Ohle; two sections on the animal fats and waxes and the fatty acids and higher alcohols, by Egon Eichwald; carotinoids and vitamin A, by Paul Karrer; cycloses, bile acids, sapotoxins, cantharidin and sex hormones, by A. Butenandt; sterols and vitamin D, by A. Lüttringhaus; two sections on amino acids and the structure and degradation of proteins, by Emil Abderhalden; three sections on acid amides, urea and guanidine, nitrogenous bases and pyrrols, imidazole and vitamin B, by F. A. Hoppe-Seyler; phosphatides and cerebrosides, by E. Klenk; sulphur-containing compounds, glutathione and insulin, by W. Dirscherl; iodine-containing compounds, by Karl Junkmann; two sections on pyrimidins, purines, nucleic acids and nucleases, by H. Steudel and O. Flössner; pigments containing pyrrol nuclei, by Hans Fischer and Karl Zeile; structure of high molecular weight combinations, by A. J. van der Wijk; polysaccharides, by Hans Pringsheim; general chemistry of proteins, by Hans Handovsky; two sections on special chemistry of proteins and degradation and derivatives of proteins, by E. Strauss and K. Burschkies; chromoproteins (respiratory pigments), by Felix Haurowitz; general treatment of animal enzymes and desmolases, by Carl Oppenheimer, esterases, phosphatases and sulphatases, by Eugen Bamann; carbohydrases, by Rudolf Weidenhagen; acylamidases, purinamidases and proteases, by W. Grossmann; arginase and histidase, by S. Edlbacher; aldehydrases and alcoholhydrases, by C. Neuberg and E. Simon; dehydrases, by T. Thunberg; tyrosinases, by L. Pincussen; heavy metal containing animal oxidases, by Karl Zeile; nonenzymic intermediary catalyzers, by B. Kisch; animal toxins, by H. Schlossberger and F. Koch, and animal pigments of unknown nature, by O. Fürth.

The second part includes three sections on Donnan equilibrium, surface tension phenomena and the colloidal state, by H. Handovsky; the biologic oxidation-reduction potential, by T. Thunberg; temperature control of living processes, by T. A. Maass; two sections on physical chemistry of enzymes and theory of the specificity of enzymes, by Karl Josephson; the mechanism of oxygen activation, by K. Zeile; mechanism of hydrogen activation, by Alfred Bertho; active iron by O. Baudisch; two sections on energy exchange of living tissue and the general treatment of energy-liberating cell reactions, by C. Oppenheimer; descriptive chemistry of the cell, by S. Edlbacher; analytic studies on pigments, by A. Nagel; the exchange of cell constituents, by E. Gellhorn; three sections on autolysis, detoxification and influence of radiations on the cell, by L. Pincussen; three sections on the Pasteur-Meyerhoff reaction, synthesis and degradation of the phosphates and carbohydrate degradation in the animal cell, by K. Lohmann; the rôle of glutathione, by E. Bumm; three sections on general treatment of carbohydrate degradation, fermentation and endo-oxidation, by Carl Neuberg with Maria Kobel and Ernst Simon; insulin and tissue metabolism, by H. Blaschko; two sections on degradation of fatty acids and degradation of amino acids, by H. A. Krebs; and the degradation of nucleic acid, by H. Steudel and O. Flössner.

The third part presents two sections on antigens and antibodies, with especial reference to toxin action and antitoxic immunity and the general principles of chemotherapy, by H. Sachs; antitoxins and toxins, by H. Schlossberger and R. Krumeich; anaphylaxis and related phenomena by Max Fränkel; four sections on agglutination, antibodies against biocolloids, serodiagnosis of syphilis, and immunity against bacteria and protozoa, by Erich Putter; bacteriophages, by R. Otto; hemolysis, by Georg Blumenthal. The division adopted for the subject matter is such that considerable repetition is certain to result. It appears that in some cases this could have been avoided to advantage. On the whole, the reviews have been made quite international in scope. Undoubtedly certain subjects not included, such as vitamin E, pituitary hormones, cortical hormone, secretin, blood chemistry and essential amino acids, will be treated in the supplements to the other volumes of the original work. The reviews as presented are valuable indeed, as one might expect in view of the international reputation of many of the specialists chosen as contributors.

Diseases of the Nervous System. By W. Russell Brain, M.A., F.R.C.P., Assistant Physician to the London Hospital and the Royal London Ophthalmic Hospital. Cloth. Price, $8.75. Pp. 899, with 51 illustrations. London: Oxford University Press, 1933.

In a book of about 900 pages there is a discussion of the whole nervous system, including the neuroses. The book has an unusual feature in that there is a discussion of diseases of the nervous system in relation to life insurance. Necessarily the discussions are short, although some of the subjects are adequately covered while many are not. The book first discusses disorders of function in the light of anatomy and physiology. It is interesting in this connection that in a discussion on pyramidal syndromes the author follows the outline of Hughlings Jackson in discussing positive and negative symp-

toms. This is an admirable attempt, but the difficulty is that in the rest of the book this is not carried out. This is a great pity, for it would have been a distinct gain to have such a division carried through a textbook on neurology. It is to be hoped that some author some day will do this.

As an example of the space given the various topics, the whole subject of aphasia is covered in nine pages, and apraxia and agnosia in two. The discussion of the fifth nerve with its diseases and method of treatment, including injection, takes up thirteen pages. The discussion is brief but adequate. The same thing can be said regarding the eighth nerve. The recognition of glossopharyngeal neuralgia is attributed to Wilfred Harris. Some years before that an American described it. Intracranial tumors take up about fifty pages. The classification of the types of lesion is that usually adopted. The discussions are cursory but cover the main points. There is a chapter on intoxications and deficiency disorders. Addiction to alcohol, morphine, cocaine and so on is discussed. It is interesting that in this group is included the discussion of polyneuritis. Injuries to the brain take fifteen pages, and this includes intracranial birth injuries. Migraine is discussed among paroxysmal and convulsive disorders. The discussion of the neuroses, which takes up twenty-four pages, is hardly adequate and it would have been better left out. Lastly, there is a useful list of references.

The day for textbooks of this sort has long since passed. It is practically impossible to cover the whole realm of neurology, including the psychoneuroses, in a book limited to 900 pages. There is not enough material for the student of medicine, certainly not for the student of neurology. On the other hand, the general practitioner might find the book useful.

The A-B-C of Refraction. By F. D. B. Waltz, M.D. Cloth. Price, $1.75. Pp. 86, with illustrations. Detroit: F. D. B. Waltz, 1933.

This is a primer intended to instruct the general practitioner in refraction with the idea of fitting glasses, using a cycloplegic instead of permitting his patients to go to an optician for manifest refraction. The author evidently labors under the delusion that retinoscopy can be learned from a textbook. If the average general practitioner attempted to fit glasses with only this textbook as a guide, his results would be no better than those of the optometrist and might have the sad effect of causing the public to lose faith in refraction under cycloplegia. Aside from ten pages of case reports, the book contains nothing not found in any good general physiology, except the author's remarks on frames, and so on. The book is of no value to a student of ophthalmology and contains nothing a medical student cannot get from his physiology. It is impossible to learn refraction properly by daily practice under a minimum of three months.

Medizinische Kolloidlehre. Herausgegeben von Prof. Dr. L. Lichtwitz, Direktor der I. Inn. Abt. des Rudolf-Virchow-Krankenhauses Berlin, Dr. Dr. Raph. Ed. Liesegang, und Prof. Dr. Karl Spiro, Direktor des Physiologisch-Chemischen Instituts der Universität Basel. Lieferung 4. Paper. Price, 5 marks. Pp. 233-304, with 10 illustrations. Dresden & Leipzig: Theodor Steinkopff, 1933.

The colloidochemical standpoint applied to the skin and the eye reveals fascinating vistas. Franz Herrmann's article on the skin starts out with a picture of a startling imitation of epithelial structure produced by droplets of silver nitrate placed at appropriate distances on a sheet of gelatin containing chloride. He discusses the hydration of the skin, the electrolytes of the skin, the manner in which the hydrogen ion concentration of the skin is changed by disease and by various remedial influences, and the distribution of the electrolytes of the mineral salts in the skin. Then he turns to the study of the true colloidal material of the skin and shows how various pathologic changes in the skin may be explained as changes in its colloid condition, in the direction either of increasing or of lessening the consistency of the gel. Knowledge of colloid chemistry is applied to the eye by F. P. Fischer in the study of the normal eye: its transparent media, its nontransparent vascular tissues, and the intra-ocular fluid with its relation to the blood serum and the membrane separating the two sols. The data thus established are then applied in a most interesting manner to the pathology of the eye. It is evident that the dermatologist as well as the ophthalmologist, in order to keep in touch with fundamentals in their respective special fields, will have to adopt the colloidochemic point of view, which may lead to as yet undreamed of developments in therapy; for the changes recorded by the pathologist may in many instances be traced to their inception by colloidochemistry, and it should be possible to apply in consequence the great therapeutic principle *obsta principiis* (check the beginnings).

Physical Treatment by Movement, Manipulation and Massage. By James B. Mennell, M.A., M.D., B.C., Medical Officer, Physico-Therapeutic Department, St. Thomas's Hospital. Third edition of "Massage: Its Principles and Practice." Cloth. Price, $6. Pp. 618, with 274 illustrations. Philadelphia: P. Blakiston's Son & Company, Inc., 1934.

The title in this edition has been changed, as the scope of the book has become much larger. The author points out to the practicing masseurs and massueses what he considers to be the rationale of massage treatment and repeatedly stresses the importance of gentleness. The main object of the book is to serve as a reference for physicians when issuing instructions to masseurs. A medical man who fails to give adequate orders may be responsible for a disappointment for which his masseur is blamed. A physician should consider the prescription of massage treatment in the same light as he would consider that of a potent drug and watch its effects no less closely, varying the dose and the nature of the dose from time to time according to indications. Manipulations and exercises must often precede, should frequently accompany and must almost invariably follow effective work by the orthopedic surgeon. The technic of massage manipulations as well as free, assisted and passive motions is given in detail; few chapters are devoted to reeducation of muscles after injuries or amputations. Massage in obstetrics and gynecology has not been overlooked. The text is profusely illustrated with numerous reproductions of photographs, roentgenograms and instructive sketches. The book is indispensable to traumatic surgeons.

Les réactions du tissu pulmonaire dans la tuberculose: Etude expérimentale et interprétation. Par E. Leuret, professeur à la Faculté de médecine, médecin des hopitaux de Bordeaux, et J. Caussimon, médecin résidant du sanatorium des hospices de Bordeaux. (Substratum anatomopathologique de l'état d'allergie.) Paper. Price, 30 francs. Pp. 85, with 55 illustrations. Paris: Masson & Cie, 1933.

The subject matter of this monograph is a familiar one to American physicians because of the large number of studies in recent years. The authors have confined their attention chiefly to French works and their own experiments. The organization of the study is simple and logical and the conclusions are clear. In general, the views expressed are already recognized on the basis of other work. The authors stress the similarity of initial reaction in the lung regardless of type of irritating agent, simple foreign body or tubercle bacilli, dead, attenuated or virulent. An interesting difference from the ordinary conception of pulmonary reaction will be noted in their emphasis on the eliminative character of the pulmonary tissue reaction. Investigators of tuberculous bacillemia and histopathologists in general will find much of interest in the authors' exposition of the part played by the polymorphonuclear leukocyte both in spreading and in combating infection.

An Outline of Immunity. By W. W. C. Topley, M.A., M.D., F.R.C.P., Professor of Bacteriology and Immunology in the University of London. Cloth. Price, $6. Pp. 415, with 37 illustrations. Baltimore: William Wood & Company, 1933.

This book is written with the avowed purpose of improving the instruction of medical students in immunity. It seems reasonable to urge that the student should be prepared to apply sound knowledge of immunity when he takes up the study of clinical medicine, and the author is firmly convinced that on account of its great practical importance immunity should receive much more attention in the medical curriculum than is the case today. It is a thorough, comprehensive, well arranged, well written, competent book on the various fundamental and practical aspects of immunity, and nevertheless it does not seem possible that the ordinary preclinical medical student can use the book to good advantage. He needs a simpler and more elementary presentation. On the other hand, for the advanced student, the teacher, the young clinician, the epidemiologist and the investigator this is the choice book on immunity at this time.

Anleitung zur Vornahme von Leichenöffnungen. Von Prof. Dr. R. Maresch, Vorstand, und Priv.-Doz. Dr. H. Chiari, Assistant, des Pathologisch-anatomischen Institutes der Universität in Wien. Cloth. Price, 3.25 marks. Pp. 114, with 17 illustrations. Berlin & Vienna: Urban & Schwarzenberg, 1933.

This is a memorial to Carl Rokitansky, who in 1834 became professor of pathologic anatomy in Vienna, and contains an excellent photograph of him as the frontispiece. The authors are director and assistant, respectively, in the same institution. The technic of postmortem examinations which they describe is essentially that instituted by Rokitansky himself. The principle of this method is to conduct the examination so as to disturb the "physiologic" relations of the organs as little as possible and, as far as is feasible, to examine each organ in situ. This method has the advantage of doing the least amount of violence to one's esthetic sensibilities. The several chapters furnish detailed instructions for the proper examination of the external features of the body; for opening the head and the investigation of its contents, including the nose and its sinuses, the orbital cavity and the middle and internal ear; for removal of the spinal cord; for examination of the organs in the thoracic and abdominal cavities, including Rokitansky's special technic for opening the heart; and for section of the extremities. A special chapter deals with the method of examining the bodies of the newly born, and another with the preparation of the body after the examination is completed. In an appendix the weights and sizes of the more important organs are tabulated according to age and sex. The authors begin their incision for opening the body at the larynx. There is no mention of the technic employed by most American pathologists of beginning the incision below the sternal notch with cross incisions below and parallel to the clavicles; or, in the case of female bodies, of beginning the longitudinal incision over the xiphoid process with a second connecting incision extending from axilla to axilla downward below the breasts. Nor is there any mention of the method of evisceration described by Le Count. But these newer methods would hardly be in place in a book which describes the technic that has been employed in one famous institution for a century. The authors' descriptions of the various procedures are clear. Many are illustrated by line drawings that are sketchy but adequate for their purpose. The volume is an excellent guide in the technic of postmortem examination but obviously cannot supply the experience necessary to the correct interpretation of the pathologic changes revealed. It emphasizes the desirability of complete necropsies properly performed.

Bentley and Driver's Text-Book of Pharmaceutical Chemistry. Revised by John Edmund Driver, Ph.D., M.Sc., A.I.C., Lecturer on Chemistry in the University College of Nottingham. Second edition. Cloth. Price, $7. Pp. 538, with 41 illustrations. New York & London: Oxford University Press, 1933.

The first edition of this book was reviewed in THE JOURNAL, June 12, 1926, page 1858. The review pointed out that the volume took up substances described in the British Pharmacopeia and was not based on the U. S. P. X and so would be of little value in this country. The present volume appears to be carefully revised and a new section added, but the criticism made in the review of the original volume is just as applicable to this book.

Weitere Beiträge zur Pathologie der traumatischen Gehirnblutungen. Von O. Berner, Pathologisk Laboratorium, Ullevål Sykehus, Oslo. Skrifter utgitt av Det Norske Videnskaps-Akademi i Oslo. I. Mat.-Naturv. Klasse. 1933. No. 5. Utgitt for Oslo Kommunes Fond. Paper. Price, 12.00 Kr. Pp. 105, with 88 illustrations. Oslo: Jacob Dybwad, 1933.

In this brief monograph the author presents the clinical and postmortem observations in forty-two cases in which death occurred subsequent to head injuries. The report is chiefly concerned with demonstrating that bleeding in the floor of the fourth ventricle and about the aqueduct of Sylvius occurs in such a high percentage of these cases as to be the rule. It is the author's opinion that such hemorrhages are the cause of death and he goes on to state that if such bleeding is absent death is in all probability due to some cause other than traumatic injury of the head. Any well considered contribution to the present inadequate knowledge of the pathology of head injuries is always welcome. There are, however, two major criticisms of this monograph that seem justifiable. This particular study might have advantageously been greatly condensed, especially the case reports, which constitute the major part, so that it would be suitable for publication in one of the current periodicals dealing with pathology or neurology. All readers familiar with the subject must entertain sincere doubts that such hemorrhage into the brain stem as the author describes is responsible for death in all cases in which death occurs as a direct result of cerebral trauma. It would seem from the author's presentation that this may readily be an important factor, but that it is the almost universal cause seems unlikely. The illustrations are for the most part satisfactory. There is no index, but in a work consisting almost entirely of case reports one is hardly necessary.

The Biology of the Protozoa. By Gary N. Calkins, Ph.D., Sc.D., Professor of Protozoölogy, Columbia University. Second edition. Cloth. Price, $7.50. Pp. 607, with 225 illustrations. Philadelphia: Lea & Febiger, 1933.

The author has not attempted to give a complete account of the protozoa, which number about 15,000, but rather to tell the story of the biology of unicellular organisms, with emphasis on such phenomena as cell division, maturity, sex differentiation and fertilization. Physicians will be especially interested in the chapter on parasitism and disease, which has been added in this edition, wherein are discussed the several hundred trypansomes found in man and animals; the amebas, which have suddenly assumed unusual significance in the United States, and the sporozoa, of which the malaria parasite is an example Besides a large bibliography at the end of the book there is a special bibliography at the end of each chapter. The illustrations, which are profuse, are mainly of free living forms.

Medicolegal

Medical Practice Acts: Electrical Treatments Administered by a Chiropractor.—Mary Miller, a licensed chiropractor, and her assistant, Nancy Kehoe, were convicted of violating the medical practice act of New Jersey. They appealed to the Supreme Court of New Jersey. The evidence disclosed that Mrs. Miller had a sign, "Dr. Mary Miller," on the window of her office and the words "Dr. Miller" on the door mat. She diagnosed the ailments of patients, prescribed a diet of food and soda as a medicine, and administered electrical treatments, which treatments were also given by Nancy Kehoe. In one instance at least Mrs. Miller directed the administration of opiates at the direction of a physician she called on the telephone. Mrs. Miller advertised herself as "Dr. Miller" under the classified list of physicians in the city directory. It is needless to say, said the Supreme Court of New Jersey, that such activities constitute the practice of medicine. The defendants contended, however, that because the act of 1920 (Pamphlet Laws, 1920, p. 15), which defined "chiropractic," was repealed, there was now no legal definition of the word, and inferentially that the scope of chiropractic practice was not limited. Even though the legislature has not since defined chiropractic, answered the Supreme Court, this fact does not deprive it of all meaning. The dictionary definition (Webster's New International) is, "The practice of adjusting the joints, especially of the spine, by hand, for the curing of disease." The judgments of conviction were affirmed.—*Miller v. New Jersey State Board of Medical Examiners (N. J.) 167 A. 740; Kehoe v. New Jersey State Board of Medical Examiners (N. J.), 167 A. 740.*

Malpractice: Hypodermic Needle Broken in Patient's Gum.—The defendant, a dentist, inserted a hypodermic needle into the plaintiff's gum, to administer an anesthetic. The needle broke and about one inch of it remained in the tissues. Operations to remove the fragment were unsuccessful, and the embedded needle, according to the patient, caused her to suffer severe pain, headaches and nervousness. The patient and her husband sued the dentist and obtained judgment. The defendant-dentist thereupon appealed to the district court of appeals, third district, California.

Over objection by the defendant, the trial court admitted testimony to prove an alleged conversation, in which the patient,

her husband and the defendant participated, and in which the defendant admitted he had made a mistake and promised to take up with his insurance carrier the matter of indemnity. Generally, said the appellate court, reference to the fact that a defendant is indemnified by a policy of insurance is prejudicial error, which cannot be cured by striking out the testimony or by an admonition to the jury to disregard it. This rule, however, does not prevent the introduction of evidence to prove a conversation, such as was testified to in the present instance, that contains an admission of responsibility, along with reference to the existence of insurance. Because the evidence of this conversation was properly admitted, there was no prejudicial error in referring to it in the argument to the jury.

The appellant dentist contended further that the trial court erred in permitting lay witnesses to testify concerning medical matters that properly could be testified to only by experts. The patient's husband was permitted, over objection, to testify that before the accident his wife was in good health physically and mentally. The lay evidence was properly admitted, said the court, citing 10 California Jurisprudence 978:

> Under one of the exceptions to the general ruling excluding the opinion of nonexperts, the opinion of such a witness derived from observation may be received in connection with his statement of the facts upon which it is based. It is said that this exception applies to questions of . . . sickness and health.

The refusal of the trial court to instruct the jury that a licensed dentist is presumed to have the skill and learning, and to exercise the judgment, required by law, and that this presumption can be refuted only by the testimony of expert witnesses, was deemed proper, because the proposed instruction ignored the right of the jury to consider the testimony of lay witnesses on matters of common knowledge, in determining the question of the defendant's negligence.

The judgment of the trial court in favor of the patient and her husband was affirmed.—*Walter v. England (Calif.), 24 P. (2d) 930.*

Medical Practice Acts: Discretion of Board in Granting Licenses by Reciprocity.—Walker was graduated by the St. Louis College of Physicians and Surgeons in June, 1922, after a four years course of instruction. At any time between the date of his graduation and June 25, 1923, when the Missouri medical practice act was amended, his professional qualifications would have entitled him to an examination by the Missouri State Board of Health, with a view to his being licensed to practice medicine in the state. He understood, however, that he would not pass the Missouri examination and determined to apply to the Arkansas eclectic state medical board for a license to practice in Arkansas. To do so it was necessary for him to have been graduated by an eclectic medical school. In April, 1923, he therefore enrolled in the Kansas City College of Medicine and Surgery. On October 12 of the same year he was granted a diploma and three days later, after an examination, he was duly licensed to practice in Arkansas. He practiced there for not less than a year.

Some time later he applied to the Missouri State Board of Health for a license to practice medicine in Missouri, to be issued by virtue of his Arkansas eclectic license, without examination. The state board of health in March, 1929, refused to grant him a license on that basis. He sought to compel it to do so by mandamus. The trial court refused to grant his petition and Walker appealed to the Supreme Court of Missouri, division No. 2. The Supreme Court found that the state board of health acted within its sound discretion in refusing a license. Persons licensed by reciprocity are granted a privilege, not of right but of good will, and in the exercise of the board's sound discretion. Walker contended that the board rejected his application arbitrarily, unreasonably and capriciously, because in January, 1929, it had granted licenses without examination to four licentiates of the Arkansas eclectic state medical board. That fact, said the court, is evidence rather of an exercise of rational discrimination such as should mark the policy of the board in the observance of the comity declared by the statute. The applications of the Arkansas physicians who were licensed by the board showed that their experience and their recommendations by Missouri physicians differed from those of Walker. Walker's testimony warranted the inference that he took the supplementary course in Kansas City only in order to be licensed in Arkansas and later to take advantage of the Missouri reciprocity statute. Reciprocity, said the court, does not countenance subterfuge.

The judgment of the trial court, denying the writ of mandamus, was affirmed.—*State ex rel. Walker v. State Board of Health (Mo.), 61 S. W. (2d) 925.*

Society Proceedings

COMING MEETINGS

Alabama, Medical Association of the State of, Birmingham, April 17-19. Dr. D. L. Manon, 519 Dexter Avenue, Montgomery, Secretary.

American Association of Genito-Urinary Surgeons, Hot Springs, Va., May 14-16. Dr. Henry L. Sanford, 1621 Euclid Avenue, Cleveland, Secretary.

American Association on Mental Deficiency, New York, May 26-29. Dr. Groves B. Smith, Beverly Farms, Godfrey, Ill., Secretary.

American Clinical and Climatological Association, Toronto, Canada, May 21-23. Dr. Francis M. Rackemann, 263 Beacon Street, Boston, Secretary.

American College of Physicians, Chicago, April 16-20. Mr. E. R. Loveland, 133 South 36th Street, Philadelphia, Executive Secretary.

American Gastro-Enterological Association, Atlantic City, April 30-May 1. Dr. Russell S. Boles, The Rittenhouse Plaza, Philadelphia, Secretary.

American Gynecological Society, White Sulphur Springs, W. Va., May 21-23. Dr. Otto H. Schwarz, 630 South Kingshighway, St. Louis, Secretary.

American Psychiatric Association, New York, May 28-June 2. Dr. William C. Sandy, State Education Building, Harrisburg, Pa., Secretary.

American Society for Clinical Investigation, Atlantic City, April 30. Dr. H. L. Blumgart, 330 Brookline Avenue, Boston, Secretary.

American Urological Association, Atlantic City, May 22-24. Dr. Gilbert J. Thomas, 1009 Nicollet Avenue, Minneapolis, Secretary.

Arkansas Medical Society, Little Rock, April 16-18. Dr. W. R. Brooksher, 602 Garrison Avenue, Fort Smith, Secretary.

Association of American Physicians, Atlantic City, May 1-2. Dr. James H. Means, Massachusetts General Hospital, Boston, Secretary.

California Medical Association, Riverside, April 30-May 3. Dr. Emma W. Pope, 450 Sutter Street, San Francisco, Secretary.

Connecticut State Medical Society, Bridgeport, May 23-24. Dr. Charles W. Comfort, Jr., 27 Elm Street, New Haven, Secretary.

District of Columbia, Medical Society of the, Washington, May 2. Dr. C. B. Conklin, 1718 M Street, N.W., Washington, Secretary.

Florida Medical Association, Jacksonville, April 30-May 2. Dr. Shaler Richardson, 111 West Adams Street, Jacksonville, Secretary.

Georgia, Medical Association of, Augusta, May 8-11. Dr. Allen H. Bunce, 139 Forrest Avenue, N.E., Atlanta, Secretary.

Illinois State Medical Society, Springfield, May 15-17. Dr. Harold M. Camp, Lahl Building, Monmouth, Secretary.

Iowa State Medical Society, Des Moines, May 9-11. Dr. Robert L. Parker, 3510 Sixth Avenue, Des Moines, Secretary.

Kansas Medical Society, Wichita, May 9-11. Dr. J. F. Hassig, 804 Huron Building, Kansas City, Secretary.

Louisiana State Medical Society, Shreveport, April 9-12. Dr. P. T. Talbot, 1430 Tulane Avenue, New Orleans, Secretary.

Maine Medical Association, Bangor, May 28-29. Miss Rebekah Gardner, 22 Arsenal Street, Portland, Secretary.

Maryland, Medical and Chirurgical Faculty of, Baltimore, April 24-26. Dr. Walter Dent Kerlin, 1211 Cathedral Street, Baltimore, Secretary.

Medical Library Association, Baltimore, May 21-23. Miss Marjorie J. Darrach, 645 Mullett Street, Detroit, Secretary.

Mississippi State Medical Association, Natchez, May 8-10. Dr. T. M. Dye, McWilliams Building, Clarksdale, Secretary.

Missouri State Medical Association, St. Joseph, May 7-10. Dr. E. J. Goodwin, 634 North Grand Boulevard, St. Louis, Secretary.

National Tuberculosis Association, Cincinnati, May 14-17. Dr. Charles J. Hatfield, Henry Phipps Institute, Philadelphia, Secretary.

Nebraska State Medical Association, Lincoln, May 22-24. Dr. R. B. Adams, Center-McKinley Building, Lincoln, Secretary.

New Hampshire Medical Society, Manchester, May 15-16. Dr. C. R. Metcalf, 5 South State Street, Concord, Secretary.

New York, Medical Society of the State of, Utica, May 14-16. Dr. D. S. Dougherty, 2 East 103d Street, New York, Secretary.

North Carolina, Medical Society of the State of, Pinehurst, April 30-May 2. Dr. R. B. McBrayer, Southern Pines, Secretary.

North Dakota State Medical Association, Fargo, May 28-29. Dr. Albert W. Skelsey, 20½ Broadway, Fargo, Secretary.

Northern Tri-State Medical Association, Flint, Mich., April 10. Dr. Herbert E. Randall, 503 South Saginaw Street, Flint, Mich., Secretary.

Oklahoma State Medical Association, Tulsa, May 21-23. Dr. L. S. Willour, Ainsworth Building, McAlester, Secretary.

Society for the Study of Asthma and Allied Conditions, Atlantic City, N. J., April 28. Dr. W. C. Spain, 116 East 53d Street, New York, Secretary.

South Carolina Medical Association, Charleston, May 1-3. Dr. E. A. Hines, Seneca, Secretary.

South Dakota State Medical Association, Mitchell, May 14-16. Dr. John F. D. Cook, Langford, Secretary.

Tennessee State Medical Association, Chattanooga, April 10-12. Dr. H. H. Shoulders, 706 Church Street, Nashville, Secretary.

Texas, State Medical Association of, San Antonio, May 7-10. Dr. Holman Taylor, Medical Arts Building, Fort Worth, Secretary.

Western Branch Society American Urological Association, Los Angeles, April 27-29. Dr. George W. Hartman, 999 Sutter Street, San Francisco, Secretary.

West Virginia State Medical Association, Huntington, May 14-16. Mr. Joe W. Savage, Public Library Building, Charleston, Executive Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to Fellows of the Association and to individual subscribers to THE JOURNAL in continental United States and Canada for a period of three days. Periodicals are available from 1925 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 12 cents if two periodicals are requested). Periodicals published by the American Medical Association are not available for lending but may be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Journal of Public Health, New York

23: 1223-1342 (Dec.) 1933

The Physician and Public Health Officialdom. M. Fishbein, Chicago.—p. 1223.
Proposed Federal Food and Drugs Act: Its Public Health Features. W. S. Frisbie, Washington, D. C.—p. 1232.
The Roentgenogram in So-Called Acute Silicosis. H. L. Sampson, Trudeau, N. Y.—p. 1237.
Pathology of So-Called Acute Silicosis. L. U. Gardner, Saranac Lake, N. Y.—p. 1240.
Silica Content of the Lungs of a Group of Tunnel Workers. C. S. Smith and Helen L. Wikoff, Columbus, Ohio.—p. 1250.
Some Factors Involved in the Use of Chloramines for Disinfection of Swimming Pools. A. H. Fletcher and E. C. Link, Memphis, Tenn.—p. 1255.
Hemolytic Properties of Mastitis Streptococcus. P. A. Hansen, G. J. Hucker and Marion A. Snyder, Geneva, N. Y.—p. 1262.
Outbreak of Erythema Infectiosum in Elmsford, N. Y. Phyllis Schuyler Kerr, New York, and E. H. Marsh, White Plains, N. Y.—p. 1271.
Pulmonary Asbestosis. J. Donnelly, Hunterarille, N. C.—p. 1275.
Has Diabetes Become More Prevalent? C. Bolduan, New York.—p. 1282.
Significance of Copper and Iron in Blood Restoration. C. A. Elvehjem, Madison, Wis.—p. 1285.
Rapid Agglutination Technic Applied to Bacillus Pertussis Agglutination. Pearl L. Kendrick, Grand Rapids, Mich.—p. 1310.

American Review of Tuberculosis, New York

28: 711-910 (Dec.) 1933

Diagnosis of Carcinoma of the Lung. L. Hamman, Baltimore.—p. 711.
Sarcoid of Boeck (Benign Miliary Lupoid), and Tuberculin Anergy: Report of Case and General Remarks. Marion B. Sulzberger, New York.—p. 734.
Treatment of Inoperable and Postoperative Urogenital Tuberculosis. S. L. Wang, New York.—p. 746.
*Treatment of Pulmonary Tuberculosis by Hyperpyrexia: Preliminary Report. G. R. Duncan, E. P. K. Fenger and A. B. Greene, Oak Terrace, Minn.—p. 752.
Collapse Therapy of Pulmonary Tuberculosis in Negroes. H. D. Chadwick, Newton, Mass.; R. C. L. Markoe, Detroit, and J. T. Thomas, Cleveland.—p. 759.
Comparative Results of Artificial Pneumothorax in the White and Negro Races. B. L. Brock, Waverly Hills, Ky.—p. 767.
Collapse Therapy of Pulmonary Tuberculosis in Negroes. A. R. Gaines and P. E. Keller, Denver.—p. 779.
Contralateral Hemoptysis in Artificial Pneumothorax: Report of Case. J. Kaminsky, Waltham, Mass.—p. 785.
Unusual Observation Following Artificial Pneumothorax. S. Simon and H. S. Abrams, St. Louis.—p. 788.
Mechanical Thorax for Experimental Study. J. J. Singer, St. Louis.—p. 791.
First-Infection and Reinfection Types of Tuberculosis. J. A. Myers, Minneapolis.—p. 793.
Significance of Tuberculous Lesions Found in Adolescent Children in a School Survey. H. W. Hetherington, Philadelphia.—p. 827.
Statistical Study of Patients Readmitted to Glen Lake Sanatorium, 1916-1931. Frances Nemec and A. E. Treloar.—p. 838.
Study of Growth in Area of Intracutaneous Tuberculin Reactions. C. A. Stewart, Minneapolis.—p. 844.
Viability and Virulence of Old Cultures of Tubercle Bacilli: Studies on Twelve-Year Broth Cultures Maintained at Incubator Temperature. H. J. Corper and M. L. Cohn, Denver.—p. 856.
Tubercle Bacilli in Blood Stream of Rabbits Following Subcutaneous and Intraperitoneal Inoculation. Lucy Mishulow and W. H. Park, New York, assisted by Nathalie Dillont.—p. 875.
Inhibitory Effect of Normal Blood on Growth of Tubercle Bacilli at Incubator Temperature. H. J. Corper and C. B. Vidal, Denver.—p. 878.
Effect of Animal Passage on Virulence of Tubercle Bacilli. H. S. Willis, Northville, Mich.—p. 884.

Treatment of Tuberculosis by Hyperpyrexia.—Of the five patients suffering from tuberculosis who were treated by hyperpyrexia, Duncan and his associates observed resolution over a period of from ten to eleven days in three, sixteen days in one, and seventeen days in the other one. The usual rise of the patient's temperature was to 104 F. or higher by mouth. The patients submitted to this treatment presented a poor prognosis. The authors state that in those patients who show improvement the treatment should be continued with rest periods intervening and, when the patient's condition warrants, at higher temperatures for a longer time. They conclude that because of their patients' poor outlook at the beginning of treatment there is some definite value in hyperpyrexia as applied to pulmonary tuberculosis and that it is possible by hyperpyrexia to show roentgen and clinical improvement in pulmonary tuberculosis in a period as short as ten days.

Annals of Medical History, New York

6: 1-94 (Jan.) 1934

Galen's Writings and Influences Inspiring Them. J. Walsh, Philadelphia.—p. 1.
Withering on Digitalis, 1785. W. T. Dawson, Galveston, Texas, and J. Chapman, Osawatomie, Kan.—p. 31.
Rabanus Maurus: "De Sermonum Proprietate, Seu De Universo." E. C. Jessup, Roslyn, Long Island, N. Y.—p. 35.
Assyrobabylonian Ophthalmology. A. C. Krause, Baltimore.—p. 42.
Medicine in Horace Walpole's Letters. R. Hutchison, London, England.—p. 56.
Johann Peter Frank and His "System Einer Vollständigen Medicinischen Polizey." Leona Baumgartner and Elizabeth Mapelsden Ramsey, New Haven, Conn.—p. 69.

Archives of Ophthalmology, Chicago

10: 733-878 (Dec.) 1933

Operative Treatment of Retinal Detachment with Electrocoagulation. A. Knapp, New York.—p. 733.
*Kahn Reaction in Aqueous Humor: Its Relation to Syphilis of the Eye. F. B. Fralick, Ann Arbor, Mich.—p. 745.
Retinal Detachment in Toxemias of Pregnancy: Report of a Case. M. Jaffe, New York.—p. 754.
Mydriatic Glaucoma: Statistical Study. S. V. Abraham, Los Angeles.—p. 757.
*Use of Nupercaine in Ophthalmology. M. K. Bochner, Toronto.—p. 763.
Visual Results in Cases of Intra-Ocular Foreign Body: Study of Two Hundred and Seventy Cases. W. F. Duggan, New York.—p. 768.
Chemistry of the Lens: V. Relation of Anatomic Distribution of Lenticular Proteins to Their Chemical Composition. A. C. Krause, Baltimore.—p. 788.
Hole in the Macula: Report of Case in a Patient Under Observation. J. W. Crawford, San Francisco.—p. 793.
Rodent or Mooren's Ulcer of Cornea: Report of Three Cases with Healing. S. R. Gifford, Chicago.—p. 800.
Leukemic Retinitis. L. J. Goldbach, Baltimore.—p. 808.

Kahn Reaction in Aqueous Humor.—Fralick presents the hypothesis that a positive Kahn reaction in the aqueous humor may be expected when the tissues from which that fluid is derived are syphilitic and that a negative reaction may be expected with a nonsyphilitic involvement of these tissues. He subjected forty-seven patients to puncture of the anterior chamber and determined the Kahn reactions in the aqueous humor, the blood and the spinal fluid. His observations substantiate the hypothesis. The most interesting exception to these observations can be expected in inadequately treated syphilitic patients showing iridocyclitis, in whom the reaction of the aqueous may be positive and that of the blood and of the spinal fluid negative. From the cases investigated which showed involvement of the posterior part of the uvea or of the optic nerve, the author could evolve no means of prediction as to the Kahn reaction in the aqueous humor. He observed no correlation between the Kahn reactions of the spinal fluid and those of the aqueous humor. He states that the Kahn test of the aqueous humor might be used as a differential diagnostic procedure in certain cases of uveitis of obscure etiology.

Use of Nupercaine in Ophthalmology.—Bochner gives a summary of his experiences with nupercaine ophthalmology over a period of three years. On the basis of his results he concludes that nupercaine is a most satisfactory anesthetic for both instillation and infiltration anesthesia in ophthalmologic practice. The maximal strength should never exceed 1 per cent for instillation and 1:1,000 for infiltration. The maximal effect does not take place for at least ten minutes after the injection or instillation, and for operations involving traction on the iris an interval of half an hour should elapse between the instillation of the first drop and the operation, unless the instillation is supplemented by a retrobulbar injection. For instillation at least from 15 to 20 drops of epinephrine hydrochloride per ounce (30 cc.) should be added to overcome the vasodilator effect. The epinephrine does not appear to increase the anesthetic action. There is only slight drying of the corneal epithelium, and no alteration in the tension or the influ-

ence on the pupil results. The action is much more prolonged than that of any other anesthetic, and the drug is relatively less toxic. In more than 2,000 cases no toxic reaction was observed when the drug was used in the strength mentioned. As a non-narcotic it lends itself readily to prescription in combination with other drugs, in the form of solutions or ointments.

Archives of Pathology, Chicago

16: 769-904 (Dec.) 1933

*Atypical Form of Paget's Disease Appearing as Generalized Osteosclerosis. H. L. Jaffe, New York.—p. 769.
*Leiomyosarcoma of the Duodenum. Dorothy H. Andersen and Elsie F. Doob, New York.—p. 795.
Primary Malignant Lymphocytoma of the Prostate Gland. D. G. Mason, Portland, Ore.—p. 803.
Avitaminosis: XVI. Production of Gastric Ulcers in the Albino Rat as a Result of Specific Influence of Deficiency of Vitamin B. B. Sure, Fayetteville, Ark., and H. S. Thatcher, Little Rock, Ark.—p. 809.
Latent Portal Cirrhosis of the Liver. J. S. McCartney, Minneapolis. —p. 817.
*Effect of Roentgen Irradiation on the Healing of Wounds. G. Ritchie, Madison, Wis.—p. 839.
Calcification of the Skin in Diabetes Mellitus. A. H. Davis and S. Warren, Boston.—p. 852.
Anatomic Mechanism in the Production of the Flint Murmur. M. Rosenthal, Brooklyn.—p. 862.

Atypical Form of Paget's Disease Appearing as Generalized Osteosclerosis.—Jaffe studied the bones from a man, aged 58, which showed advanced osteosclerosis, markedly intense in certain areas. The calvarium, spine, innominate bones, sternum and ribs were investigated; the long tubular bones could not be examined. Although Paget's disease was not plainly suggested in the gross, except possibly in the ilia, the microscopic studies led to the conclusion that the changes in the bones were those of Paget's disease. The histologic appearances were not similar to the typical mosaic arrangement of florid Paget's disease. The author concluded that the slow evolution of the pathologic changes was the reason for the absence of a mosaic arrangement such as appears in typically florid areas of Paget's disease. The slow progress of the disease permitted healing to keep almost abreast with its evolution. Furthermore, the slow progress of the evolution of the disease and the concomitantly rapid healing led to the production of osteosclerosis rather than to the usual gross changes of Paget's disease. A somewhat similar case was described by Schmidt but was erroneously interpreted as osteosclerotic anemia. The relation of this condition to Pick's endosteal Paget's disease is not clear. Thus, Paget's disease may appear in atypical form, the bones, in the gross, evidencing generalized osteosclerosis.

Leiomyosarcoma of the Duodenum.—Andersen and Doob report a case of duodenal leiomyosarcoma with symptoms referable to repeated hemorrhage into the intestine for five years, compression of the inferior vena cava for seven weeks and a palpable tumor in the right side of the abdomen for six weeks. The tumor compressed the inferior vena cava, and thrombi were formed in the common iliac veins. Death resulted from pulmonary embolism. The authors analyze this case and the eighteen other cases of leiomyosarcoma of the small intestine that have been reported in the literature.

Roentgen Irradiation and the Healing of Wounds.—Ritchie presents the results of an experimental investigation of the effect of roentgen rays on the healing of wounds, with a brief review of the experimental and clinical literature on the subject. The early histologic features found in such irradiated wound tissue are: (1) sluggishness of fibroblastic growth, (2) the presence of anomalous giant fibroblasts and (3) the persistence of a fibrin network for a varying period. The first of these is considered to be most important from a practical point of view and is most consistently seen when irradiation follows incision by approximately twenty-four hours. The second is the most constant characteristic, and, since it has been noted also in human tissues subjected to roentgen and radium treatment, the author thinks that its presence in inflammatory tissue is highly suggestive of a reaction to roentgen rays. It is obviously improper to carry the results of animal experimental work bodily and in detail over into clinical practice; such an investigation can be seen in its true light only when thoroughly checked by clinical observation. Nevertheless enough evidence has accumulated to warrant the statement that roentgen irradiation in doses ordinarily used for the treatment of malignant tumors, administered within forty-eight hours after incision, may definitely retard healing but has no bad effect as far as ultimate results are concerned.

Iowa State Medical Society Journal, Des Moines

23: 649-706 (Dec.) 1933

Surgical Clinics. H. M. Richter, Chicago.—p. 649.
Appendicitis: Its Increasing Mortality. G. M. Crabb, Mason City. —p. 652.
How Can the Present Mortality from Appendicitis Be Lowered? C. L. Heald, Sigourney.—p. 656.
The Perforated Appendix. F. W. Mulsow, Cedar Rapids.—p. 660.
Possibility of Earlier Diagnosis and Treatment of Hepatic Cirrhosis. A. M. Snell, Rochester, Minn.—p. 661.
Nephritis in Childhood. M. J. Foster, Cedar Rapids—p. 668.
Bronchiectasis. M. L. Floyd, Iowa City.—p. 668.
Bronchoscopy. J. A. Downing, Des Moines.—p. 669.

Journal of Immunology, Baltimore

23: 461-534 (Dec.) 1933

Species of Specificity of Fibrinogens. H. B. Kenton, Chicago.—p. 461.
Survival of Neurotropic Yellow Fever Virus in Testicular Tissues. W. Lloyd and A. F. Mahaffy, Lagos, Nigeria, Africa.—p. 471.
*Comparative Value of Tuberculoprotein (MA 100) and Old Tuberculin, with Especial Reference to Sensitization. J. D. Aronson and Rae V. Nicholas, Philadelphia.—p. 483.
Streptococcus Leukocidin. F. P. Gay and Florence Oram, New York. —p. 501.

Comparative Value of Tuberculoprotein and Old Tuberculin.—The results that Aronson and Nicholas obtained with small amounts of freshly diluted old tuberculin and tuberculoprotein (MA 100) show a close agreement, but with larger amounts a larger percentage reacted to the old tuberculin than to tuberculoprotein. When those who failed to react to old tuberculin and to tuberculoprotein were retested approximately three months later, a small proportion reacted to the old tuberculin but a larger proportion reacted to tuberculoprotein. In a high percentage of those retested with tuberculoprotein, evidence of sensitization was given by the appearance of the specific inflammatory reaction (Arthus phenomenon) at the site of injection.

Journal of Pharmacology & Exper. Therap., Baltimore

49: 387-592 (Dec.) 1933. Partial Index

Question of Elimination of Barbituric Acid Derivatives in the Urine, with Especial Reference to Iso-Amyl Ethyl Barbituric Acid (Sodium Amytal) and *l*-Methyl-Butyl Ethyl Barbituric Acid (Pentobarbital Sodium). H. A. Shonle, A. K. Keltch, G. F. Kempf and E. E. Swanson, Indianapolis.—p. 393.
Studies of Effect of Ultraviolet Rays on Nicotine. V. A. Gant, Chicago. —p. 408.
Bradycardia Caused by Sympathomimetic Drugs. L. Terry and H. C. Peters, Chicago.—p. 428.
Studies of Chronic Morphine Poisoning in Dogs: V. Recovery of Morphine from Tissues of Tolerant and Nontolerant Animals. O. H. Plant and I. H. Pierce, Iowa City.—p. 432.
*Absorption of Insulin from Intestinal Tract. D. Campbell and T. N. Morgan, Aberdeen, Scotland.—p. 450.
Hyperglycemic Action of Certain Drugs. D. Campbell and T. N. Morgan, Aberdeen, Scotland.—p. 456.
Influence of Caffeine on Effects of Acetanilid. J. A. Higgins and H. A. McGuigan, Chicago.—p. 466.
Studies on Calcium: IX. Further Observations on Acute Thrombophlebitic Edema. A. L. Lieberman and N. R. Cooperman, Chicago. —p. 479.
Experimental Investigation on Treatment of Toxemia: Part II. G. N. Myers, Cambridge, England.—p. 483.

Absorption of Insulin from Intestinal Tract.—Campbell and Morgan demonstrated that once insulin gets into the portal circulation it is just as active as when given into the systemic circulation. This fact, taken along with the observation that insulin is not rapidly destroyed in the intestine, indicates that the main reason for the failure of insulin to act when administered orally is that it is not absorbed from the intestine. The difficulty appears to lie in the selective absorptive power of the intestinal mucosa. The authors attempted to facilitate the absorption of insulin by combining it with lecithin. The compound formed is soluble in ether, is presumably of the nature of an adsorption compound, is active on subcutaneous injection, but is not absorbed from the alimentary canal either of the rabbit or of man.

Kansas Medical Society Journal, Topeka

34: 457-492 (Dec.) 1933

The Health Officer and the General Practitioner. W. H. Young, Fredonia.—p. 457.
Some Experimental Work with Rabies. G. E. Finkle, Canton.—p. 460.
*Results of Treatment of Intermittent Claudication and Thrombo-Angiitis Obliterans with Parathormone: Report of Four Cases: Preliminary Report. D. V. Conwell, Halstead.—p. 465.

Treatment of Intermittent Claudication and Thrombo-Angiitis Obliterans with Parathyroid Extract.—Conwell treated two patients having intermittent claudication and two having thrombo-angiitis obliterans with parathyroid extract-Collip. The indications for its trial were no improvement with other forms of treatment employed previously and the presence of a hypocalcemia suggesting a metabolic disturbance with possible vasoconstrictor hyperirritability. Two of the patients were facing certain amputation. The parathyroid extract was given in amounts of 0.5 cc. or 10 units subcutaneously every other day for ten injections. The improvement was relatively rapid and uniform. The attacks of intermittent claudication were controlled, permitting at least a temporary return to normal activity. The circulatory changes in the patients having thrombo-angiitis obliterans were prompt and there was a complete control of the pain that had necessitated morphine, return of warmth, moisture, diffuse reddish hue on elevation of the foot, loss of tenderness, improved sensation and motion of the toes, disappearance of the ecchymoses and deeper discoloration, and there was a return of the pulse in the dorsalis pedis and the posterior tibial arteries. There were no untoward reactions. Calcium gluconate was given by mouth to two patients and not given to the other two, but their responses appeared to be equal. The calcium of the blood plasma dropped slowly in one case.

Kentucky Medical Journal, Bowling Green

31: 549-588 (Dec.) 1933

Indications for Cesarean Section from Surgeon's Point of View. D. P. Hall, Louisville.—p. 551.
Cancer of the Breast. W. O. Bullock, Lexington.—p. 555.
Hernia into the Paraduodenal Fossa with Large Biliary Calculus: Report of Case. I. A. Arnold, Louisville.—p. 561.
Cancer of the Colon. F. W. Rankin, Lexington.—p. 563.
Medical Preparation of a Patient for Urologic Surgery. F. M. Stites, Jr., Louisville.—p. 567.
Acute Suppurative Otitis Media and Its Complications. G. W. White, Henderson.—p. 569.
Use of the Roger Anderson Well Leg Counter Traction Splint in Fractures of the Neck of the Femur. O. R. Miller, Louisville.—p. 573.
Treatment of Burns. C. Baron, Covington.—p. 579.
Jaundice. J. D. Hancock, Louisville.—p. 580.

Medical Annals of District of Columbia, Washington

3: 1-28 (Jan.) 1934

Accidents and Injuries: Comparative Study of Their Causes Among Various Groups. J. P. H. Murphy, Washington.—p. 1.
Volvulus: Review with an Illustrative Case. W. B. Marbury and E. M. Pickford, Washington.—p. 7.
Cleidocranial Dysostosis: Report of Case. J. R. Cavanagh, Washington.—p. 11.
Fundamentals of Internal Medicine: Diseases of the Heart. W. M. Yater, Washington.—p. 13.

Medical Bull. of Veterans' Adm., Washington, D. C.

10: 79-172 (Oct.) 1933

Residual Effects of Warfare Gases: Use of Arsenical Compounds, with Report of Cases. H. L. Gilchrist and P. B. Matz.—p. 79.
Thrombo-Angiitis Obliterans: Report of Fifty-Two Cases. E. T. Evans and A. G. Dumas.—p. 99.
Triorthocresol Phosphate Poisoning Due to Ingestion of Adulterated Jamaica Ginger. O. P. Goodwin.—p. 110.
Intracranial Pressure: Its Diagnosis by Roentgen Methods. B. A. Moxness.—p. 115.
Heart Block. R. S. E. Murray.—p. 120.
Group Blood Pressures. H. Caldwell.—p. 124.
Pulmonary Asbestosis. G. A. Stock.—p. 126.
Prescnile Psychoses. W. M. Bevis.—p. 130.
Pleurisy with Effusion and Its Relation to Tuberculosis. E. D. Hatch.—p. 133.
Treatment of Pleurisy with Effusion in Pulmonary Tuberculosis. J. L. Lewis.—p. 138.
Critical Review of Use of Cod Liver Oil and Irradiated Ergosterol in Treatment of Tuberculosis. G. D. Guilbert.—p. 141.
Bronchial Asthma. E. A. Montague.—p. 145.
Suggestions for Effecting Economies in Medical Procedures. G. W. Phillips.—p. 149.
Review of Forty Edentulous Cases. C. S. Lister.—p. 151.

Medicine, Baltimore

12: 355-446 (Dec.) 1933

*Porphyrins in Human Disease. V. R. Mason, C. Courville and E. Ziskind, Los Angeles.—p. 355.

Porphyrins in Human Disease.—Mason and his associates base their study on the clinical observations of four patients presenting the acute, idiopathic type of hematoporphyria, and also on the postmortem examination of the tissues of two of these patients who died from involvement of the nervous system with symptoms closely resembling acute ascending paralysis of the peripheral nerve type. They discuss the distribution and the chemical properties of the porphyrins and their relation to disease in human beings. No specific therapeutic measures have been found. Patients having the dermal type of the disease should be protected from the injurious rays of the sun and those having the acute toxic or acute idiopathic type of the disease must be treated symptomatically. Since the porphyrins form insoluble salts with calcium, this element should be given in some form, although its therapeutic value is not yet known. The authors discuss the chemistry of porphyrins, the clinical features, symptomatology, pathologic anatomy, pathogenesis, and so on, as they pertain to porphyrins in the human being.

New England Journal of Medicine, Boston

209: 1191-1254 (Dec. 14) 1933

Pelvic Inflammation: Course and Treatment and Elliott Treatment. F. C. Holden, New York.—p. 1191.
Placenta Praevia: Review of Four Hundred and Thirty-Seven Cases from the Boston Lying-In Hospital. F. S. Kellogg, Boston.—p. 1201.
*The Use of Pituitary Extract in Obstetrics. C. R. Alden, Boston.—p. 1211.
Malignancy of the Colon. C. L. Smart, Laconia, N. H.—p. 1216.
Latest Developments of the Tonsil Problem. A. J. Provost, Manchester, N. H.—p. 1221.
Management of Congestive Cardiac Failure. C. H. Beecher, Burlington, Vt.—p. 1226.
Varicose Veins and the Injection Treatment. G. P. Pennoyer, New York.—p. 1228.
Studies of Reproduction in the Rat: III. Vitamin E—Neutralized When Mixed with Lard. D. Macomber, Boston.—p. 1235.

209: 1255-1314 (Dec. 21) 1933

Appendices Epiploicae: Their Surgical Significance with Report of Three Cases. D. C. Patterson, Bridgeport, Conn.—p. 1255.
Physiology of Pulmonary Circulation. H. L. Blumgart, Boston.—p. 1259.
Pathologic and Clinical Aspects of Pulmonary Circulation. P. D. White, Boston, and O. Brenner, Birmingham, England.—p. 1261.
Pulmonary Embolectomy. E. C. Cutler, Boston.—p. 1265.
Types of Edema and Their Treatment. H. A. Christian, Boston.—p. 1267.
Gastric Syphilis Simulating Carcinoma of Stomach: Case. B. Kaplan, New Bedford, Mass.—p. 1270.
Observations on Use of Paraffin Oil Preparations. R. L. Patterson and C. M. Jones, Boston.—p. 1275.
Studies of Reproduction in the Rat: IV. Occurrence of Spontaneous Amputation in Young Growing Rats Whose Mothers Were on Certain Diets. D. Macomber, Boston.—p. 1277.
Amebic Abscess of the Liver Without Preceding Diarrhea: Case Report. L. S. McKittrick, Boston.—p. 1280.
Toxemias of Pregnancy: Critical Review of Recent Literature. D. Hurwitz, Boston.—p. 1281.

Use of Solution of Pituitary in Obstetrics.—In discussing the use of solution of pituitary in obstetrics, Alden refers to the solution that contains 10 international units per cubic centimeter. In multiparas, when slight contractions have been established, 2 ounces (60 cc.) of castor oil and 15 grains (1 Gm.) of quinine bisulphate are given. Half an hour later, 5 grains (0.3 Gm.) of quinine bisulphate is given, followed in half an hour by a hot soapsuds enema and in half an hour by the intramuscular injection of 2 minims (0.12 cc.) of solution of pituitary, which is repeated at half hourly intervals for six doses, provided labor does not start in the meantime. The administration of solution of pituitary is stopped as soon as the patient is in labor. In primiparas the amount of solution of pituitary is reduced to 1 minim (0.06 cc.). For uterine inertia during the first stage of labor, solution of pituitary may be given in doses of 1 minim. Excessive use of solution of pituitary during the first stage of labor will result in tetanic contraction of the uterus and may rupture the body of the uterus, the lower uterine segment or the cervix. A hot bath will often relieve the tetanic contraction, or deep etherization may be instituted. During the second stage of labor, solution of pituitary may be used in doses of from 0.5 to 1 cc. Repetition of the dose may

cause a distinct shutting down of the uterine musculature about the child. Once the placenta is expelled, the routine intramuscular injection of the full dose of 1 cc. of solution of pituitary is indicated, followed by, or coincident with, an injection of ergot. When bleeding is not controlled by one dose or when there is late relaxation of the uterus, a 1 cc. dose of solution of pituitary may be repeated, the possibility of a so-called pituitary reaction being kept in mind. In cesarean sections, solution of pituitary is of value in causing the uterus to shut down and in controlling bleeding after the extraction of the baby. Intramuscular or intravenous injection is employed chiefly. The intramuscular injection is made at the moment of incision into the uterus. If intravenous injection is used, it should be decided on in the beginning and not given on top of one or two intramuscular injections. It should not be given before and not too long after the extraction of the baby. It may be diluted with from 5 to 10 cc. of physiologic solution of sodium chloride and should be given slowly. Solution of pituitary in conjunction with ergot is of value in cases of subinvolution of the puerperium, when from 4 to 8 minims (0.25 to 0.5 cc.) is given three times a day. Solution of pituitary stimulates the unstriped muscle fibers of the intestine and bladder in atonic conditions. In postoperative distention following cesarean sections, it may be administered every four hours in full doses. An intramuscular injection of solution of pituitary given half an hour previously will increase the efficiency of enemas in intestinal paresis. Retention of urine during the puerperium due to atony of the traumatized bladder is often favorably influenced by repeated injections of solution of pituitary intramuscularly three times a day. Solution of pituitary is contraindicated in cases of toxemia with high blood pressure, nephritis, myocarditis and arteriosclerosis.

New Jersey Medical Society Journal, Orange

30: 817-878 (Dec.) 1933

*Recurrent Vomiting: Clinical Study. F. I. Krauss, Chatham.—p. 823.
Carcinoma of the Small Intestines. S. A. Goldberg, Newark.—p. 828.
Newer Radiologic Methods of Gastro-Intestinal Examination: Critical Evaluation and Practical Survey Based on Personal Experience. R. Pomeranz, Newark.—p. 831.
Conservative Management of Chronic Middle Ear Suppuration. O. R. Kline, Camden.—p. 837.
Genito-Urinary Tuberculosis. S. R. Woodruff, Jersey City.—p. 841.
Surgery of Kidney and Ureter in Infants and Children. M. F. Campbell, Montclair.—p. 845.
Lead Absorption and Lead Poisoning: Clinical and Pathologic Analysis of One Hundred Cases. O. Lowy and L. J. Levinson, Newark.—p. 849.
Preoperative Treatment in Gynecology. W. J. Carrington, Atlantic City.—p. 854.
*Scarlet Fever Immunization by Inunction: Preliminary Report. M. L. Ripps, Elizabeth.—p. 858.
Death Rates of New Jersey State Hospital at Marlboro, Fiscal Year Ending June 30, 1933. H. G. Borden, Marlboro.—p. 861.

Recurrent Vomiting.—Recurrent vomiting in childhood, according to Krauss, is usually of a neuropathic origin and should be treated primarily by a study of the constitution of the child. Avoidance of physical and especially nervous fatigue is most important. Change in dietary habits with a reduction in the amount of pure carbohydrates and starches and with a relative increase in the amount of fats predisposes, in a certain type of child, to an accumulative, periodic toxemia characterized by persistent vomiting and prostration. It is most common in children from 2 to 7 years of age and is seldom seen after the age of 10. As the child grows older the mother becomes less insistent on the quantity of milk taken, and more pure carbohydrates are allowed. This automatically corrects the tendency to recurrent toxemia, which these patients possess. Other predisposing causes are physical defects in the intestinal tract and chronic infection, especially in the tonsils. Attacks are precipitated by acute infections and by physical and mental exhaustion. Treatment of the metabolic imbalance by reduction of the fat and increase of the carbohydrates will clinically cure the majority of the cases. The acute attack, if severe, demands the liberal injection of fluids, preferably physiologic solution of sodium chloride or dextrose solution, until vomiting is controlled and diuresis is well established.

Scarlet Fever Immunization by Inunction.—Ripps states that, of 112 Dick positive children completing treatment, fifty-seven were rendered negative from eighteen to nineteen weeks after the last inunction. Cold cream inunction proved superior to hydrous wool fat in that it was quicker to absorb and produced a larger percentage of immunizations. The children who gave the most marked reactions to the Dick test were the most difficult to immunize. In children from 1 to 4 years of age the results were poor, only 33 per cent of the subjects in this group having been rendered negative. A higher percentage of immunization may, perhaps, be obtained with increasing dosage. As much as a 90,000 skin test dose of toxin has been given to a group without any reaction. Because of the ease of administration and lack of reaction, a continued study of this method of immunization should be made.

Northwest Medicine, Seattle

32: 491-540 (Dec.) 1933

Loyalty to the State Organization. A. E. Mackay, Portland, Ore.—p. 491.
New Deal in Relationship of the Physician to Organizations Dispensing Free or Part-Pay Medical Service. S. G. Henricks, Portland, Ore.—p. 493.
Experiments in Hospital Insurance. R. W. Nelson, Portland, Ore.—p. 498.
The Aims, Organization and Operation of Professionally Controlled Group Health Associations. E. P. Owen, Portland, Ore.—p. 500.
Tumors of Colon and Rectum. A. T. Bazin, Montreal.—p. 503.
*Spastic Paraplegia (Little's Disease): Treatment by Repeated Cisternal Drainage. N. W. Clein, Seattle.—p. 507.
Arthritis: Its Dietary Treatment. W. E. Gatewood, Portland, Ore., and Leila Wall Hunt, Pullman, Wash.—p. 511.

Treatment of Spastic Paraplegia by Repeated Cisternal Drainage.—Clein performed repeated cisternal drainage in ten cases of spastic paraplegia. The infants have shown sufficient benefits to warrant a continuation of this type of treatment. Four were hopeless automatons, and drainages were performed merely to relieve distressing symptoms. Of the remaining six, one child, now 4 years of age, walks, runs and talks almost as well as other children of his age. When 22 months old he could not sit up, talk or recognize people or objects. His condition can be made much worse in a few days' time by increasing his fluid intake from 10 to 25 or 30 cc. He becomes listless and nervous and he tires easily. If he urinates larger quantities, he improves; otherwise, he remains listless and dull. Cerebrospinal fluid drainage and limitation of his fluids result in marked improvement within a few days. Improvement seems more rapid in the few cases in which treatment was begun at the age of from 15 to 24 months than in those of from 8 to 15 months. The author does not wish to leave the impression that this method of treatment is a cure for Little's disease but that it has greatly improved several children and relieved others of distressing symptoms.

Philippine Islands Med. Association Journal, Manila

13: 541-586 (Dec.) 1933

Tetralogy of Fallot: Report of Case with Necropsy. A. Liboro and J. S. Hilario, Manila.—p. 541.
Lymphatic Absorption of Iodized Ethyl Esters of Wightiana Oil by Intramuscular Injection. J. O. Nolasco, Culion.—p. 552.
Morbid Mental Trends of the Major Psychoses Among Filipinos. T. Joson, Rizal.—p. 557.
Cirrhosis of the Liver Among Filipinos: Notes. B. Barrera, Manila.—p. 562.

Public Health Reports, Washington, D. C.

48: 1543-1584 (Dec. 29) 1933

Experimental Studies on Acute Mercurial Poisoning. S. M. Rosenthal.—p. 1543.

Science, New York

79: 1-18 (Jan. 5) 1934

Method for Studying Drought Resistance in Plants. H. L. Shirley.—p. 14.
*Modified Sabouraud Medium Suitable for Cultivation of Acid-Fast Actinomycetes. Sara A. Scudder, New York.—p. 16.

Modified Sabouraud Medium for Cultivation of Acid-Fast Actinomycetes.—Scudder isolated an acid-fast strain of actinomycetes from the blood in a case of acute mastoiditis complicated by sinus thrombosis, septicemia and arthritis by means of a modified formula of French proof agar. This strain was non-acid fast on such mediums as the standard Bordet-Gengou, potato, synthetic phosphate and Difco Sabouraud. The formula that the author employs consists of 4 per cent maltose, 1 per cent Difco peptone and 1.8 per cent flaked agar dissolved

in unfiltered beef heart or veal infusion instead of water. No adjustment in reaction is made. Glycerin and other carbohydrates may be added if desired. Slanted agar favors development of acid fastness in about four days. A grayish brown powdery substance develops on the upper portion of the slant simultaneously with the appearance of the acid-fast portions of growth. The acid-fast component appeared in young cultures (seventy-two hours) on this medium as branching non-acid-fast mycelia containing acid-fast pleomorphic portions. Old cultures consisted of non-acid-fast oval components and mycelia interspersed with acid-fast oval components. The acid-fast characteristic was inhibited on all other mediums.

South Carolina Medical Assn. Journal, Greenville

29: 269-296 (Dec.) 1933

Cataract. I. J. Mikell, Columbia.—p. 273.
Treatment of Traumatic Tetanus: Report of Six Cases. C. O. Bates, Greenville.—p. 276.
Interesting Problem in After Care of Hemorrhoidectomies. T. Brockman and S. Cain, Jr., Greenville.—p. 281.

Southern Surgeon, Atlanta, Ga.

2: 1-96 (March) 1933

Central or Intracapsular Fractures of Neck of Femur. W. C. Campbell, Memphis, Tenn.—p. 1.
Treatment of Infections and Carbuncles of Face and Lips. H. A. Gamble, Greenville, Miss.—p. 24.
*Treatment of Bartholin's Gland Abscess. W. S. Dorough, Atlanta, Ga.—p. 29.
Endothelial Sarcoma of Lymph Nodes: Report of Case. W. L. A. Wellbrock, Rochester, Minn.—p. 31.
Consideration of Causes of High Mortality in Cesarean Section. J. W. Bourland, Dallas, Texas.—p. 34.
Multiple Primary Malignant Growths. I. Abell, Louisville, Ky.—p. 39.
Surgical Care of Infantile Paralysis. E. L. Scott, Birmingham, Ala.—p. 47.
Electrosurgical Unit as an Aid in the Removal of Brain Tumors and in Drainage of Brain Abscesses. C. Bagley, Jr., Baltimore.—p. 51.
Benign Tumors of the Kidney. H. E. Simon, Birmingham, Ala.—p. 67.
Use of Perfringens Antitoxin in Treatment of Paralytic Ileus. J. K. Quattlebaum, Savannah, Ga.—p. 74.
Surgery of the Larynx. M. Equen, Atlanta, Ga.—p. 79.

Treatment of Abscess of Bartholin's Gland.—Dorough, in treating abscesses of the glands of Bartholin, exposes the gland by traction after the field of operation is made ready by the usual preparation and use of antiseptics and applies a drop of phenol to the mucous membrane just inside the mucocutaneous margin. As the area is tender, a few drops of a 1 per cent solution of procaine hydrochloride are injected into the tissue overlying the abscess by means of a fine hypodermic needle, entering through the anesthetized spot. This needle is then withdrawn and a large caliber one is inserted through the anesthetized area into the cavity of the abscess. With a syringe attached, the pus is withdrawn from the cavity and the amount removed is noted. By placing the gloved finger within the vaginal orifice and exerting gentle pressure, the operator is able to evacuate the cavity almost entirely. The syringe is detached and replaced by another syringe containing hexylresorcinol. The equivalent of one-half the amount of pus removed is injected into the cavity. This may be injected and then aspirated, washing out the cavity, but in all cases this amount is left in the cavity. The patient is then instructed to sit in hot water for a few minutes as soon as convenient and to repeat this each morning and night for two or three days. A preparation of foreign protein is then injected into the gluteal muscle. The next day the inflammation has markedly subsided and it may not be necessary to repeat the procedure. If the procedure is repeated, it is rarely necessary to use any anesthetic for the insertion of the needle. As soon as tenderness subsides, the usual hot antiseptic douches are begun.

Western J. Surg., Obst. & Gynecology, Portland, Ore.

41: 663-718 (Dec.) 1933

Factor of Spasm in Etiology of Peptic Ulcerations. M. E. Steinberg, Portland, Ore.—p. 663.
End-to-End Reduction in Fractures of the Lower Extremity. R. Anderson, Seattle.—p. 671.
Simple and Efficient Pneumatic Tourniquet. C. F. Eikenbary and J. F. LeCocq, Seattle.—p. 679.
Obstetric Shock Following Delivery. R. A. Bartholomew, Atlanta, Ga.—p. 681.
Tumors of the Neck. J. E. Else, Portland, Ore.—p. 685.
Twelve Years' Experience in Organized Group Practice: Plan in Action. R. Brown, Santa Barbara, Calif.—p. 695.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Journal of Radiology, London

6: 705-768 (Dec.) 1933

Physiologic Leukocyte Counts and Detection of Small Deviations from the Normal. R. H. Simpson.—p. 705.
Radiology of Heart Disease: (A) Technic of Cardiology. J. V. Sparks.—p. 723.
Id.: (B) Teleradiographic Mensuration of the Heart. F. G. Wood.—p. 732.
Addison's Disease Radiographically Confirmed: Three Cases. A. E. Payne.—p. 747.

British Medical Journal, London

2: 1103-1152 (Dec. 16) 1933

So-Called Acidosis in Children. R. Miller.—p. 1103.
*Clinical Recognition of Structural Disease of Peripheral Vessels. G. W. Pickering.—p. 1106.
*Studies on Etiology of Blood Diseases: Pathogenic Agent in Normal Human Bone Marrow. U. Friedemann and A. Elkeles.—p. 1110.
Addison's Disease: Case. H. S. Stannus.—p. 1112.
*Treatment and Control of Essential Hypertension: New Therapeutic Measure. H. O. Gunewardene.—p. 1114.

Clinical Recognition of Disease of Peripheral Vessels.—Pickering believes that an essential step in understanding most disorders of the peripheral circulation is first to determine whether any structural lesion of the vessels is present. The author discusses the methods that he has found most serviceable in identifying structural disease of the vessels. In the absence of severe anemia, abnormal pallor of an extremity indicates emptiness of the minute vessels. Increased depth of color is due to a dilatation of the capillaries and venules of the skin as a result of injury. Postural changes in skin color are common in structural disease of the vessels but are by no means confined to these. Conspicuous pallor of the skin when a limb is raised and maintained for a few minutes above the level of the heart is strongly suggestive of a structural lesion of the vessels; and the height at which such pallor occurs is used by Buerger as an index of the degree of disease. The rate at which color returns to skin that has been blanched by pressure is frequently used as an index of the rate of the cutaneous blood flow. It is an unreliable test, because the return of color is often from the surrounding venous plexuses rather than from arteries, and the rate of return then depends chiefly on the pressure in those plexuses. An important indication of the adequacy of the blood flow through a limb is the temperature of the surface of the limb, but skin temperature has wide fluctuations in health. The air temperature necessary to produce vasodilatation and warm extremities varies from subject to subject. Coldness of the extremities does not suffice for the diagnosis of arterial disease or arterial spasm. Of greater significance is an inequality of temperature between two symmetrical limbs similarly treated and exposed for the same length of time. Although it is the rule for a limb more affected by structural vascular disease to be persistently colder than its fellow, the reverse is occasionally found. When the limb having the more affected vessels is the warmer, some other factor must be called to account for this. Pulsation may be retained in one or more of the main vessels of the foot or hand after the smaller arteries have become extensively diseased and the circulation to a limb may be almost normal in the absence of pulsation in its vessels, as is the case in the legs of patients with coarctation of the aorta. Allen has described a simple method for recognizing an organic obstruction of the ulnar or radial artery at, or distal to, the wrist. In extremities that have been warmed by immersion in water at from 42 to 45 C. (107.6 to 113 F.) for ten minutes, it is usually possible in normal subjects to elicit capillary pulsation in the palmar surfaces of the hands and plantar surfaces of the feet by light pressure with a glass slide. The presence of capillary pulsation indicates that the arteries and arterioles supplying the corresponding area of skin are patent. The veins share in the general vascular relaxation produced by warmth, and the most satisfactory method of demonstrating the superficial venous plexus is to immerse the foot for ten minutes in water at from 35 to 40 C. (95 to 104 F.) and then to distend the veins by obstructing them in the leg with pneumatic pressure of from 60 to 70 mm. of mercury.

Etiology of Blood Diseases: Pathogenic Agent in Human Bone Marrow.—The experiments of Friedemann and Elkeles demonstrated that in normal human bone marrow there is an agent which causes an encephalitis if injected intrathecally into rabbits. This agent cannot be one of the common bacteria, since all sterility tests have proved negative. The fact that the agent was present in all specimens of normal human bone marrow tested demonstrates that generally the agent is nonpathogenic for man, but this does not exclude the possibility that under some special conditions this agent may become pathogenic for man and cause disease. Their attempts to transmit the encephalitis from rabbit to rabbit through an indefinite series have had indifferent success.

Essential Hypertension.—Although unwilling to accept the theory on which the treatment of Cyriax in cases of moderately high blood pressure was based, Gunewardene modified his method by substituting electrical stimulation of the skeletal muscles and submitting patients with high grades of pressure to treatment on these lines. As a preliminary, the patients were tested to see what effect the resulting muscular contractions had on the pulse rate, particularly as some of them were on the verge of cardiac failure. In every case the pulse rate dropped, sometimes by eight beats to the minute. The results indicate that in some cases of hyperpiesia the blood pressure drops to normal figures, without rest or medicinal aid; there is also relief from distressing symptoms. In other cases there is relief from symptoms but pressures will not fall. These cases show impaired renal function as gaged by the urea concentration test. It is difficult to give an explanation of the mechanism by which the reduction of pressure is brought about.

Irish Journal of Medical Science, Dublin

No. 96: 643-698 (Dec.) 1933

Hodgkin's Disease. J. McGrath.—p. 643.
Novissima Idea de Febribus of Jacobus Sylvius. T. P. C. Kirkpatrick.—p. 667.
Pulmonary Tuberculosis Among Outpatients. G. Bewley.—p. 679.

Medical Journal of Australia, Sydney

2: 777-808 (Dec. 9) 1933

Medical Evidence, Certificates and Fees Under the Workers' Compensation Act. R. M. Mackay.—p. 777.
Diabetes Mellitus. E. Downie.—p. 784.

2: 809-836 (Dec. 16) 1933

Tubal Block and Other Adnexal Lesions from Aspect of Sterility. S. C. Fitzpatrick.—p. 809.
Lead Poisoning. G. C. Willcocks.—p. 813.
*Basophilia and Lead Excretion in Lead Poisoning. C. Badham.—p. 816.
Queen Charlotte's Hospital Report on Puerperal Fever: Summary with Some Comments. F. A. Nyulasy.—p. 821.
Position of Urinary Bladder. H. Flecker.—p. 823.

Basophilia and Lead Excretion in Lead Poisoning.—According to Badham, lead poisoning is present when the first pathologic sign of the action of lead can be detected, and this is the presence of stippled red cells. Lead poisoning with disability is present when there is anemia in mild or severe degree, evidenced by a reduction of the red cells and hemoglobin and the presence of stippled red cells with or without symptoms of lead poisoning, such as malaise, constipation, joint pains and abdominal pains. If the patient is examined in the critical period for making a diagnosis of lead poisoning, that is, when lead anemia is present, punctate basophilia is always found, and this sign is practically specific for lead poisoning. Before making a diagnosis of lead poisoning, evidence of a lead intake should be sought; and this is to be found in a knowledge of industrial processes or in the amount of lead in the urine, or from the presence of a blue line.

South African Medical Journal, Cape Town

7: 811-846 (Dec. 23) 1933

Reflections. A. F. Stewart.—p. 811.
Matters of Opinion. T. Wooldridge.—p. 812.
Cancer: I. Significance of Study of Neoplasms in Animals. G. de Kock.—p. 817.
Id.: II. Early Diagnosis of Cancer. C. G. L. van Dijk.—p. 820.
Id.: III. Early Treatment of Cancer: Surgical and Nonsurgical. W. Welchman.—p. 823.
Id.: IV. Statistics of Cancer. E. H. Cluver.—p. 825.
Id.: V. The Problem of Cancer. J. A. Orenstein.—p. 827.

Presse Médicale, Paris

42: 185-208 (Feb. 3) 1934

Allergy to Tuberculin and to Tuberculous Ultravirus Filtrates, Compared. G. Paisseau, J. Valtis and F. Van Deinse.—p. 185.
*My Method of Spinal Anesthesia with Nupercaine. B. Quarella.—p. 187.
Glandular Cheilitis: Precancerous State of the Lower Lip. Touraine and Solente.—p. 191.

Spinal Anesthesia with Nupercaine.—Quarella describes the technic that he uses for spinal anesthesia with nupercaine. Patients are prepared one hour before the operation by an injection of a freshly prepared ampule containing 0.0006 Gm. of scopolamine hydrobromide, 0.015 Gm. of morphine hydrochloride and 1 cc. of a 10:100 aqueous solution of mannite. The dose may be adjusted depending on the age and condition of the individual patient. Fifteen minutes before the anesthetic the patient is given one or two ampules of ephedrine (each containing 0.05 Gm.) subcutaneously, the dose depending on the blood pressure of the patient and the level of anesthesia to be obtained. The technic of anesthesia involves the following steps: drawing into the syringe of from 1.4 to 2 cc. of a 1:200 solution of anesthetic, the amount depending on the general condition of the patient and the level of anesthesia to be obtained; spinal puncture of the patient in a sitting position and at a level between the twelfth thoracic and fifth lumbar vertebra; removal of from 5 to 10 cc. of spinal fluid depending on the pressure and level of anesthesia to be attained; aspiration into the syringe containing the anesthetic of from 6 to 8 cc. of spinal fluid; slow subarachnoid injection of the contents of the syringe; in cases of high spinal anesthesia, repetition of the aspiration of spinal fluid and reinjection, but with a lesser quantity; putting the patient quickly flat on the table with the head raised on a cushion in a more or less inclined position depending on the level of anesthesia to be reached; and waiting fifteen minutes at least, and twenty or twenty-five in cases of high anesthesia, for the effect to be profound before starting the operation. The author believes that this technic compares favorably with other methods and other anesthetics. One of the special advantages of nupercaine rests in its short period of activity when introduced into the subarachnoid space, which limits its danger due to excessive diffusion.

Policlinico, Rome

41: 57-120 (Feb. 1) 1934. Medical Section

Effects of Venesection on Chemical and Physiochemical Constitution of Blood. P. Steffanotti.—p. 57.
*Action of Hydrochloric Acid on Glycemia of Hepatic Patients. A. M. Michelazzi.—p. 78.
Research on Chronaxia of Muscles and Peripheral Nerves in Cardiac Patients. G. Borruso.—p. 96.

Action of Hydrochloric Acid on Glycemia of Hepatic Patients.—Michelazzi studied the effect of hydrochloric acid on the glycemic curves of patients presenting hepatic lesions. He made four separate glycemic curves, after administration of dextrose, of dextrose and hydrochloric acid, of water and of hydrochloric acid alone. The dosages were 100 Gm. of dextrose and 80 drops of the official solution of hydrochloric acid. The dextrose was dissolved in 200 cc. of water and given to the patient on a fasting stomach. The hydrochloric acid was diluted in small quantities of water and given by mouth. The author found that the administration of hydrochloric acid causes a marked diminution in glycemia. This diminution is not uniform as to quantity but is always demonstrable and may attain high values. In one case there was a maximum rise of the glycemic curve to 63 mg. per hundred cubic centimeters of blood, as compared to the curve obtained with dextrose only, while in another case the glycemic curve was lowered 70 mg. In all cases the lowering of the glycemic curve was more intense and more constant in the alimentary curves than in those obtained during fasting. In one patient the maximum glycemic diminution was 22 mg. during fasting and after administration of hydrochloric acid and dextrose rose to 63 mg. The hypoglycemia due to hydrochloric acid may be explained by the synergistic action of internal and external secretion of the pancreas. The hydrochloric acid, which physiologically stimulates the pancreatic secretion, may cause a formation of secretin, once it comes in contact with the duodenal wall; this in time may induce an excitation of the function of the pancreatic acini which may be followed by the passage into circulation of

a larger amount of insulin. The action of insulin, activating the enzyme secretion of the stomach and of the pancreas, the action of acid gastric juice on the pancreatic function and vice versa, and the belief that there exists in diabetic patients a gastric hypo-acidity and pancreatic hypofunction have convinced the author that the mechanics of direct stimulation of insulin secretion is the most probable explanation of the hypoglycemic action of hydrochloric acid.

Prensa Médica Argentina, Buenos Aires

21: 113-154 (Jan. 17) 1934

Prolonged Priapism Caused by Myelogenous Leukemia: Case. C. Bonorino Udaondo, J. E. Carulla and F. Cabarrou.—p. 113.
Abscesses of Lungs. R. Finochietto.—p. 116.
Aneurysmal Dilatation of Left Auricle. C. Rodrigué.—p. 118.
*Posterior Route in Apicolysis Without Muscular Section: Technic. A. J. Pavlosky.—p. 139.
Painful External Tibial Bone. A. Lago Garcia and A. L. Masucci. —p. 142.

Apicolysis Without Muscular Section.—Pavlosky performs apicolysis and filling without muscular section by means of a vertical incision 8 cm. long beginning at the level of the transverse apophysis of the eighth cervical vertebra and proceeding downward to the specified length. This incision is made midway between the spinal apophyses and the border of the scapula. The skin, subcutaneous cellular tissue and superficial fascia are incised and drawn sideways 3 or 4 cm. The aponeurosis is cut transversely and the muscle is separated following the direction of its fibers. The muscle is retracted, exposing the bundles of the rhomboideus, the fibers of which are separated in the center of the incision by the same maneuver used for the trapezius. The serratus minor posterior superior is then in view and its fibers appear in an oblique direction from above downward and from inside outward. The fibers are separated in the same direction and in the manner used for the other muscles. The three muscles (which cover the third and fourth ribs) are retracted. The resection of the third rib, the apicolysis and the filling are performed according to the usual technic. The muscular planes are reconstructed by approximating the muscles with small No. 00 catgut sutures. Perfect anatomic restitution is thus obtained. The operation is performed under local anesthesia by infiltration.

Deutsche medizinische Wochenschrift, Leipzig

60: 123-158 (Jan. 26) 1934. Partial Index

*Leanness and Tendency to Emaciation. G. von Bergmann.—p. 123.
Biologic Action of Roentgen and Radium Rays and Their Practical Effect in Combat of Cancer. Englmann.—p. 127.
Prognosis of Laryngeal Carcinoma. C. von Eicken.—p. 130.
Is Roentgen Irradiation of Cancerous Bone Metastases Justified? A. Pickhan.—p. 132.
*Treatment of Allergic Disturbances with Skin Extract. Annemarie Köhler.—p. 136.
*Practical Aspects of Most Important Infectious Diseases. C. Hegler. —p. 138.
Necessity of Bacteriologic Control Examinations of Raw Milk to Be Pasteurized. W. Pfannenstiel and H. J. Jusatz.—p. 141.

60: 159-196 (Feb. 2) 1934

*Leanness and Tendency to Emaciation. G. von Bergmann.—p. 159.
Fate of Patients During Crisis Following Gastric Resection. F. W. Lapp and H. Neuffer.—p. 164.
Epidemic Vertigo in Bulgaria. S. Wateff.—p. 167.
Problem of Acquired and Hereditary Hypersusceptibility to Specific Poisons. R. Otto.—p. 169.
Epidemic (Lethargic) Encephalitis Following Influenza: Case. Schmidt. —p. 171.
Inhalation Therapy in Bronchial Asthma. A. Welzel.—p. 172.
Fractures of Spinous Processes. Bofinger.—p. 173.

Emaciation.—Von Bergmann considers the most important and most frequent form of emaciation a condition that has been referred to as "hypophyseal emaciation." He admits that the anterior lobe of the hypophysis may seem intact but points out that its internal secretion may be deficient, that there may be a pluriglandular disturbance and that the entire regulatory system may be impaired. He is convinced that the anterior hypophysis and the adjoining mesencephalic region are the most important factors in this form of emaciation. The patients lack appetite. Pain in the epigastric region and vomiting are often present, but the latter often yields to treatment with preparations of the anterior hypophysis. The pain in the epigastric region may lead to erroneous diagnoses and even to laparotomy. The basal metabolism is often reduced, so that, if the food intake should be normal, obesity might be the result. The intermediate metabolism is likewise subnormal. The administration of small amounts of insulin may produce severe hypoglycemic conditions. Forced feeding with insulin and dextrose is inadvisable, but dextrose alone may be given. The blood pressure is generally reduced. The majority of the author's patients were young women, in many of whom the menarche was belated, psychic difficulties set in, lack of appetite led to emaciation and often menstruation ceased. He also observed that the temperature is frequently below normal and the pulse slow. Hair growth, particularly the axillary and the pubic, is generally normal and there are no disturbances in the libido. Although there is a lack of appetite, the patients often have an abnormal craving for sour and piquant foods, particularly raw cucumbers, tomatoes and sour fruits. The author thinks that such appetites may indicate a hunger for vitamin C. A sojourn in high altitudes may be helpful. The author considers endocrine preparations most effective, particularly the extracts of the anterior hypophysis.

Treatment of Allergic Disturbances with Skin Extract.—The preparation used by Köhler is an aqueous extract of the skin. The treatment was first suggested by Milbradt. It has a specific character and does not involve any danger. As indicated in a number of case reports, the author employed it successfully in bronchial asthma, hay fever and urticaria, but the treatment failed in a case of cold urticaria. The author administered by intravenous injection up to 10 cc. daily. Later the doses may be decreased and the intervals prolonged. During the administration of the maximal doses, attention should be given to focal reactions (increased allergic reaction to irritation). The treatment with skin extract is contraindicated in patients with exophthalmic goiter, because the maximal doses of skin extract increase the action of the thyroid. The treatment should be individualized carefully. The author admits that the material in which she tried this method is rather small, but she thinks that the favorable results justify further trials.

Klinische Wochenschrift, Berlin

13: 161-200 (Feb. 3) 1934

Lipoidoses. S. J. Thannhauser.—p. 161.
*Spring Eosinophilia: Contribution to Bioclimatology of Winter-Spring Relation. B. de Rudder.—p. 167.
Do Liver and Lung Function as Blood Depots? T. Sjöstrand.—p. 169.
Acute Anterior Poliomyelitis: Pathology of Cerebrospinal Fluid. O. Rehn.—p. 173.
*Relations of Secretion of Gastric Juice to Localization of Zones of Hyperesthesia. F. Winkler.—p. 174.
Problem of Derivation of Urinary Pigment from Hemoglobin and Hematin. R. Nothhaas.—p. 176.
*Simple Method for Determination of Fructose in Blood. R. Stöhr. —p. 179.
Sodium Citrate in Hemophilia. E. Kaufmann.—p. 179.
Color Reaction for Demonstration of Glutathione in Crystalline Lens. F. P. Fischer and V. Fischl.—p. 180.
Determination of Carbon Dioxide on Thermochemical Basis. A. Thurnherr.—p. 180.
Meteorological-Physical Problems of Meteoropathology. E. Flach.—p. 181.

Spring Eosinophilia.—It is pointed out by de Rudder that Moro ascribed the action of spring on the organism primarily to the increased sympathetic sensitivity. This heightened sensitivity of the sympathetic nervous system during spring seems more understandable in view of certain factors that play a part in the pathogenesis of rickets and tetany. The author calls attention to the lack of a certain portion of the ultraviolet rays, the Dorno rays, in the pathogenesis of rickets. In normal persons the sensitivity of the sympathetic nervous system can hardly be measured directly, but it seemed reasonable to investigate whether these changes in the irritability might perhaps be detectable in the number of eosinophils in the blood, since it is this type of cell that apparently has the closest relation to the sympathetic nervous system. The author studied the number of eosinophils in thirty-three normal persons. He found that the January values of from 0 to 2 per cent had advanced by March to from 2 to 4 per cent, and in the succeeding months, when the irritating action of spring had subsided again, the values decreased once more to those present during the winter. In experiments on guinea-pigs it could be shown that the spring eosinophilia is the result of the renewed exposure to the Dorno radiation after a prolonged existence in the absence of ultraviolet rays. The author thinks that the reappearance of the Dorno rays after their prolonged absence during the winter months probably play the most important part in the bioclima-

tology of spring, for they produce an "irritation," to which even the healthy organism responds in various ways.

Secretion of Gastric Juice and Localization of Zones of Hyperesthesia.—Winkler calls attention to the observations of Head, Mackenzie and others that visceral disorders produce hyperalgesia in the cutaneous areas that are innervated by the same segments as the diseased organ. Porges was able to observe in subacidity and anacidity, which he ascribes to gastritis of the body of the stomach, that the zone of hyperalgesia is on the left side, whereas in hyperacidity, which he ascribes to gastritis of the antrum, the sensitive points are on the right side. Since the localization of the hyperalgesic zones may have a certain diagnostic significance for the secretory action of the stomach, the author decided to compare the zones of hyperalgesia with the results of the examination of the gastric juice in a large number of patients with gastritis. He was able to corroborate the observations of Porges, for he found that reduced gastric secretion is accompanied by hyperesthesia on the left side and hypersecretion by hyperalgesia on the right side, in the region of the last thoracal segments. This indicates that in hypo-acidity the body of the stomach (innervation from the left side) and in hyperacidity the antrum (innervation from the right side) is diseased. He thinks that exceptions to this rule are indicative of complicating disturbances in the region of the segments adjoining the zone of hyperesthesia.

Determination of Fructose in Blood.—Stöhr describes a simple titrimetric method for the determination of fructose, for which 0.2 cc. of blood or 2 cc. of Folin-Wu filtrate is necessary. Fructose, in contradistinction to dextrose, reduces the phosphorus-molybdic acid reagent, prepared according to Folin-Wu or Folin to a blue compound, which in turn is titrated stainless in the cold with hundredth normal potassium permanganate. The test is made on the deproteinized blood filtrate, which is prepared either according to Folin-Wu or according to Hagedorn-Jensen in the modification of Steinitz and Riesen. The reduction of the phosphorus-molybdic acid reagent is proportional to the fructose concentration. The process is not strictly specific, since dioxyacetone, methylglyoxal, glycerin aldehyde, ketol and acetol likewise have a reducing effect on phosphorus-molybdic acid. However, since these compounds do not occur in the blood under normal conditions, they do not interfere with the determination of fructose in experimental fructosemia. Dextrose produces only a minimal reduction, which in the computation is given consideration as the "blind value." The author gives the formulas of the equations that are used for the computation.

Medizinische Klinik, Berlin

30: 149-184 (Feb. 2) 1934

Diagnosis and Therapy of Extramenstrual Genital Hemorrhages. H. Siebke.—p. 149.
*Carbohydrate Metabolism in Essential Hypertension, Acromegaly and Simmond's Disease (Hypophyseal Cachexia). E. Kylin.—p. 153.
Therapy of Dermal Leishmaniosis. H. Löhe.—p. 158.
Radium Treatment of Cicatricial Keloids. H. Fuhs.—p. 160.
Experiences with Pain Reducing Measures During Delivery. O. Wallis.—p. 161.
*Value of Kauffmann's Test for Determination of Cardiac Function. E.-E. Bauke.—p. 163.
Intra-Urethral Tuberculin Reaction. F. Marquardt.—p. 164.
Early Diagnosis of Malignant Tumors. R. Links.—p. 165.
Fracture of Head of Femur or Myositis Ossificans? H. Engel and G. Seefisch.—p. 168.

Carbohydrate Metabolism in Hypertension, Acromegaly and Simmond's Disease.—According to Kylin, sugar tolerance tests show that the blood sugar content increases more in diabetes without hypertension than in normal persons, whereas the increase in hypertension diabetes is about the same as in normal persons. Diabetes without hypertension reacts to insulin tolerance tests with a more pronounced reduction than is the case in diabetes with hypertension. A blood sugar increasing counter reaction develops much earlier in diabetes with than without hypertension. As two different hormonic actions regulate the blood sugar content, namely, a reducing factor (insulin action) and an increasing factor (action of anterior hypophysis and of suprarenals), it appears that in the diabetes with hypertension the counterinsular hormones exert the stronger influence. The demonstration of the counter-insular, prehypophyseal hormone (Lucke, Houssay, Evans) seems to make possible an explanation of the differences in the reactions in diabetic patients with and without hypertension. The author assumes that the form of diabetes found in essential hypertension is generally caused by a prehypophyseal hyperfunction. He does not deny the possibility that in some cases of essential hypertension with diabetes the latter may be the result of arteriosclerotic processes in the pancreas. He calls attention to research that indicates the presence of a special type of diabetes in acromegaly, which is ascribed to overproduction of a blood pressure increasing hormone of the anterior hypophysis. In Simmond's disease, however, in which there exists an atrophy of the pituitary body, the blood sugar values are generally subnormal.

Kauffmann's Water Test for Determination of Cardiac Function.—Bauke disagrees with Zimmermann's complete rejection of Kauffmann's water test (described in the *Medizinische Klinik* **29:**1437 [Oct. 20] 1933, and abstracted in THE JOURNAL, Dec. 23, 1933, p. 2088). The author shows that Heilbronner's modification of Kauffmann's original technic gives much more reliable results. Heilbronner administers the first 150 cc. of fluid not at 7 a. m., but rather at 9 or even 10 a. m. However, even with the improved technic the outcome of the water test alone should never be considered sufficient evidence for a cardiac or circulatory insufficiency but should be considered so only in the presence of other clinical symptoms. The water test should be judged with the same caution and criticism as an electrocardiographic record, which alone would never be considered sufficient evidence of a cardiac lesion. The author recommends the combined use of electrocardiography and the Kauffmann-Heilbronner water test.

Monatsschrift f. Geburtshülfe u. Gynäkologie, Berlin

98: 183-246 (Feb.) 1934

Abortion and Sterility. L. I. Bublitschenko.—p. 183.
*Cerebral Pressure in Eclampsia: Etiology of Convulsions. G. Spoljanskij and A. Juželevskij.—p. 190.
Acute Hemorrhagic Myositis. F. Sommer.—p. 200.
*Microscopic Observation of Blood Sedimentation (Kriele): Its Utilization in Prognosis and Differential Prognosis of Septic Infections of Genital Origin. W. Thierfelder.—p. 204.
Differential Diagnosis of Narrow Pelvis. F. Kühlbacher.—p. 216.

Cerebral Pressure and Convulsions in Eclampsia.—Spoljanskij and Juželevskij employed an especially constructed manometer to determine the pressure of the cerebrospinal fluid in patients with eclampsia and found it to be within normal limits. The normal pressure in the region of the cisterna magna is + 150 mm. of water if the person is lying down. If the person sits up, the pressure is negative. An increase in the lumbar pressure is not always accompanied by an increase in the cerebral pressure. Since nearly all the patients were under chloroform anesthesia while the pressure was tested, the authors determined the influence of chloroform anesthesia on the pressure of the cerebrospinal fluid and found that it effects no reduction in the pressure. Withdrawal of cerebrospinal fluid reduces the pressure in the subarachnoidal space, no matter at what level the fluid is withdrawn. The authors conclude that their observations did not corroborate the theory that eclamptic convulsions are the result of increased intracranial pressure.

Microscopic Observation of Sedimentation.—Thierfelder points out that the microscopic observation of sedimentation by means of Kriele's chamber gave hope that it would permit a reliable prognosis in septic infections. According to Kriele the prognosis is unfavorable (1) if the leukocytes show either conglomeration or increased adhesion or (2) if the thrombocytes show either conglomeration or are reduced to less than 120,000. The author shows that the behavior of the leukocytes in microscopic sedimentation cannot be utilized for the prognosis. With regard to the thrombocytes he agrees with Kriele in that he considers a reduction to less than 120,000 unfavorable, but he considers conglomeration a favorable sign rather than an unfavorable one as Kriele did. The author further discusses the differential diagnostic possibilities of the microscopic observation of sedimentation. He found that lymphogenic sepsis is readily differentiated with the method. In the eleven cases studied he always observed thrombocyte numbers of over 180,000 and in most instances of over 200,000. The leukocytes were diffused in the plasma column and never showed a pronounced conglomeration. Observations on six patients with thrombo-

phlebitic sepsis convinced the author that in this condition Kriele's method does not come up to expectations. For the early diagnosis of puerperal peritonitis, Kriele's method is important. In this condition the symptomatology is usually not clear in the beginning, and by the time the typical symptoms appear the process has advanced so far that surgical intervention comes too late to be of any value; but the author was able to corroborate Kriele's observation of thrombocytosis, the thrombocytes reaching values of over 400,000. However, he does not agree with Kriele on the sedimentation of the thrombocytes in puerperal peritonitis, for he often noted that the thrombocytes were more dense in the upper layers. There are three points that are important in order to obtain correct results: 1. The chamber must be exactly filled and no blood cells should escape over the rim. 2. The blood should not stand longer than two hours. 3. The blood should not be withdrawn during anesthesia, and pipets and syringes should never be cleaned with ether or alcohol. The correct estimation of the sedimentation picture requires a certain amount of experience.

Münchener medizinische Wochenschrift, Munich

81: 117-156 (Jan. 26) 1934

History and Epidemiology of Influenza. H. Reichel.—p. 117.
*Present Aspects of Influenza. W. Berger, H. Seemayer and J. Schnetz.—p. 119.
Pathologic Anatomy of Influenza. H. Beitzke.—p. 125.
Influenza and Campaign Against It During Childhood. A. Reuss.—p. 127.
*Encephalitis and Influenza. M. de Crinis.—p. 130.
Surgery and Influenza. E. Seifert.—p. 133.
Herpes Zoster and Herpetic Diseases in Region of Ear. L. Haymann.—p. 137.
Significance of Orthopedics for Public Health. F. Lange.—p. 140.
Technic of Tanning of Living Tissues. F. Haustein and R. Jäger.—p. 143.
Sealing of Containers Used for Transportation of Specimens of Blood and Cerebrospinal Fluid. R. Krumeich.—p. 144.

Present Aspects of Influenza.—From observations on influenza cases that occurred in Graz during 1933, Berger and his associates conclude that the clinical aspects of influenza today differ only quantitatively from those that were observed during the influenza pandemic of 1918, in that the symptoms are less severe. However, in the various smaller influenza epidemics that have occurred since 1918, the symptomatology has reached considerable degrees of severity more frequently than was the case after 1889-1890. As before 1918, the greater danger to the higher age groups has now again taken the place of the life threatening, hyperergic disease of the younger persons, which predominated in 1918. The hemorrhagic tendency and the involvement of the lungs, pleurae and sinuses are subject to regional differences during the same epidemic, but, on the whole, they are now considerably milder than in 1918. The qualitative differences of the symptomatology (neuralgias, dyspepsias and so on) when compared to the pandemic are hardly greater than the regional differences within the same epidemic. The tendency to leukopenia increases proportionately to the degree of contagiosity. Rare forms of influenza, such as arterial thromboses, gastro-intestinal influenza or encephalitis, occur, provided there is a sufficiently large number of cases. Considering the symptomatology, there is not the least doubt that the disorder that occurred in greater and smaller epidemics since 1918 is the same disease entity as that of the pandemic of 1918.

Encephalitis and Influenza.—De Crinis discusses the general nervous symptoms that begin or accompany an attack of influenza, which, he thinks, are largely manifestations of serous meningitic irritations. However, if in the course of an influenza there develop manifestations that indicate disturbances in the cerebral parenchyma, the condition is designated influenzal encephalitis. The latter begins with general symptoms, occasionally with delirium or comatose conditions. According to the different locations of the foci, monoplegia, hemiplegia or aphasia may occur alone or in combination. The author points out that influenza may involve the peripheral nervous system in the form of a neuritis, which may appear without signs of encephalitis being present and may develop during the acute phase of the disease as well as during the period of convalescence. The relations between influenza and epidemic encephalitis have not been completely explained as yet, but the author emphasizes that epidemic encephalitis differs from influenzal encephalitis clinically, in its pathologic anatomic aspects and in its mode of dissemination. The treatment of influenzal encephalitis should be directed against the influenza. He recommends treatment with convalescent serum. Autohemotherapy in combination with antipyretics and with milk injections should be tried. Intravenous injections of methenamine have also been found helpful.

Zeitschrift für Tuberkulose, Leipzig

69: 321-400 (Feb.) 1934

Specific Prophylaxis and Therapy of Tuberculosis. M. Klimmer.—p. 325.
*Klimmer's Tuberculosis Vaccine M 44 in Treatment of Tuberculosis of Bones and Joints. B. Köppe.—p. 339.
*Experiences with Klimmer's Tuberculosis Vaccine M 44 in Prophylaxis of Tuberculosis. G. Hebel.—p. 355.
Practical Suggestions for Exact Determination of Therapeutic Results in Tuberculosis. C. Coerper.—p. 358.

Treatment of Tuberculosis of Bones and Joints.—Köppe treated nineteen cases of tuberculosis of the bones and joints with Klimmer's vaccine. In eleven cases he gained the impression that the vaccination produced a decisive turn in the course of the treatment. In six cases it was not certain whether the vaccinations exerted an influence, and two were not suitable for the estimation of the treatment, but not a single case was unfavorably influenced.

Klimmer's Vaccine in Prophylaxis of Tuberculosis.—According to Hebel's experience, Klimmer's tuberculosis vaccine is harmless. Of forty-eight children whom he vaccinated, forty-seven remained free from tuberculosis in spite of the fact that they were exposed to tuberculous infection. In four instances one each of the nonvaccinated parents developed tuberculosis, while the vaccinated children remained free from the disease. Of three children who, as controls, were not vaccinated, one contracted tuberculosis of the bones, while the five siblings, who were exposed to the same extent but had been vaccinated, remained free from tuberculosis. The author realizes that the material is too small to arrive at a definite conclusion about the prophylactic value of the vaccine, and he thinks that the specific immunization should never be the ground for the neglect and omission of the methods that have proved their worth, such as isolation of the patients, whenever it is possible, correct treatment of the sputum and improvement of the general condition by better nourishment. However, a specific remedy is nevertheless desirable, provided it is harmless.

Zentralblatt für Gynäkologie, Leipzig

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Treatment of Carcinoma of Neck of Uterus. H. Martius.—p. 305.
*Technic of Extraperitoneal Cesarean Section. G. Kaboth.—p. 310.
Rapid Delivery According to Delmas and Modification of This Method. A. Ostréil.—p. 325.
Course of Delivery in Old Primiparas. E. Redenz.—p. 331.
Weight and Length of Twins. F. Lüdi.—p. 344.
*Etiology of Cervicovaginal Laqueatic Fistulas. K. Welsch.—p. 347.
Obstetric Complications in Velamentous Placenta. H. Nöldeke.—p. 351.

Extraperitoneal Cesarean Section.—In the last five years, 308 extraperitoneal and 160 intraperitoneal cesarean operations were performed at Kaboth's clinic. He gives a detailed description of the procedure that he follows in the extraperitoneal method. In opening the abdominal wall, the attainment of a secure cicatrization should be kept in mind. The cutaneous incision and the division of the fascia are in the longitudinal direction, but the cutaneous incision is higher up toward the umbilicus, while the fascial section is made lower down toward the symphysis. The author describes the exposure of the neck of the uterus in an area large enough to permit the passage of the head. The lower pole of the peritoneal sac must be pushed upward and the bladder toward the side. Because of the frequent dextroversion of the uterus, the entire intervention is best made to the left of the median line, so that the bladder can be shifted toward the right. The cervical incision, delivery and uterine suture are the same as in case of the intraperitoneal procedure. Following completion of the uterine suture and after the removal of the blood clots, the peritoneal sac and the bladder fall into place. Drainage of the precervical space should be done through a special opening. A dressing forceps is pushed forward from the inside, and where it reaches the abdominal wall an incision is made (2 cm.) and a strip of gauze is introduced into the precervical space. The drainage

opening is at the external rim of the abdominal rectus. Thus the abdominal incision proper is not used for the drainage. In discussing the results of the extraperitoneal method the author emphasizes that the maternal mortality was smaller than in the intraperitoneal method in spite of the fact that the material in which the extraperitoneal procedure was followed had more unfavorable cases. He considers the extraperitoneal method the least trying for the mother, and he recommends it for all cases in which delivery by abdominal section is necessary.

Etiology of Cervicovaginal Laqueatic Fistulas.—Welsch relates two clinical histories that illustrate how cervicovaginal laqueatic fistulas may be caused by the introduction of laminaria bougies. In one case the laminaria were introduced for the purpose of completing an abortion. They slipped into the uterus and because of an anteflexion their external ends pressed against the posterior cervical wall. A pressure necrosis developed, rectal tenesmus set in and led to severe straining and finally the posterior cervical wall was perforated and the bougies protruded into the posterior vaginal vault. A cervicovaginal laqueatic fistula would have developed but the bridge between the perforation and the external uterine os was divided immediately after the uterus had been evacuated. The second patient was a woman in whom laminaria bougies were introduced for the treatment of dysmenorrhea. The fistula was not discovered until four years later, when she asked advice because of sterility. The author cites three other cases from the literature in which laminaria bougies caused laqueatic fistulas in the cervix. He advises against the ambulatory use of laminaria bougies.

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Substitution of Hallucinations in Meningo-Encephalitis. V. N. Ruskikh.—p. 12.
Brain Tumors with Rapid Course. D. A. Rabinovich and P. Ya. Shindelman.—p. 18.
*Acute Febrile Syphilis of Brain. N. A. Popov and G. D. Aronovich. —p. 27.
*Tuberculous Meningitis of Adults. A. I. Rozenboym.—p. 36.
Material for Study of Aphasia. M. E. Sobol.—p. 45.

Acute Febrile Syphilis of Brain.—Popov and Aronovich report six cases of acute febrile syphilis of the brain. They believe that it deserves consideration as a special form of neurosyphilis. The disease is characterized by an acute or subacute onset followed by exacerbation of symptoms. The symptoms in the beginning are grave but the response to antisyphilitic treatment is prompt. The development of the disease is not dependent on the duration of the syphilitic infection. It occurs predominantly within the first few years and even months of the syphilitic infection. Clinically two types may be distinguished: the purely meningeal and the meningo-encephalitic. The specific etiology is recognized from the history and the presence of humoral reactions in the blood and the cerebrospinal fluid. The Wassermann reaction was sharply positive in their cases. The pleocytosis of the cerebrospinal fluid may be pronounced, with a predominance of polymorphonuclear neutrophils. The histopathologic picture is one of meningo-encephalitis with a predominance of meningeal alterations. The entire process may be regarded as a flare up of a chronic meningeal syphilis.

Tuberculous Meningitis of Adults.—Rosenboym reports twenty-two cases of tuberculous meningitis of adults verified at necropsy. He concludes that tuberculous meningitis may occur at any age. The incidence of the disease was most pronounced in February and in May. The peculiarity of the tuberculous meningitis of the adults consists in the prominence of the symptoms of headache and vomiting. Other signs of meningeal irritation, particularly that of Kernig, are less pronounced. In adults, tuberculous meningitis is more frequently associated (68 per cent of the author's material) with general miliary tuberculosis. The isolated form was seen in *22* per cent of the cases. The author has not seen an isolated form in children. Tuberculous meningitis both in adults and in children is a secondary disease. The primary focus in childhood is seen most frequently in the lymph nodes, while in adults it may be found in the various organs, but most frequently in the lungs. The spread of infection in adults takes place most probably by the hematogenous route.

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*Technic of Cautery of Endopleural Adhesions According to Jacobæus, with Short Report on Results. A. Tuxen.—p. 129.
*Hemolysis in Pregnancy and Abortion (Pregnancy Toxicosis? Quinine Intoxication?). F. Harbitz.—p. 152.
*Pathologic Significance of Asymmetrical Sacralization of Fifth Lumbar Vertebra. R. Ingebrigtsen.—p. 161.
Malignant Granulocytopenia (Agranulocytosis, Schultz Type): Casuistic Report. R. Opsahl.—p. 164.
*Microsedimentation Reaction with Landau's Pipet. S. Frostad.—p. 170.
Case of Hypochloremia with Azotemia. O. I. Olsen.—p. 178.

Cautery of Endopleural Adhesions.—Tuxen says that endopleural adhesions are present in three fourths of all cases of pneumothorax. Moderately extensive adhesions or adhesions over the stronger part of the lung may offer so slight an obstacle to collapse that the pneumothorax does become effective; with extensive unfavorably situated adhesions, a partial pneumothorax results. Thoracocauterization is indicated on clinical-roentgenologic signs of ineffective pneumothorax, and even in clinically effective pneumothorax roentgenologic adhesions over the cavern or preventing selective collapse constitute a strong indication for cauterization. With intended or performed bilateral pneumothorax, cauterization of every fairly easily divided adhesion is called for. Roentgen examination does not give exact information as to location, extent or character of the adhesions, and the feasibility of thoracocauterization must be determined by thoracoscopy. Thinner threads and strands and membranes at a good distance from the lung are easily operated on; thick pedicles, membranes close to the lung, hour-glass adhesions and thin, finger-like pedicles with short or no fibrous transition to the chest wall are difficult to operate on. Difficult adhesions are divided only on strict clinical-roentgenologic indication. If the grave finger-like pedicles cannot be divided, pneumothorax should be discontinued and thoracoplasty done instead. Flat adhesions cannot be operated on. The time of operation should not be earlier than two months after pneumothorax; with too long delay, exudation may render the procedure more difficult. Long, thin, solitary threads should be divided early. In ninety-two cases of thoracoscopy in Tuxen's material, follow-up information was available. In the seventy-nine cases of ineffective pneumothorax thoracocauterization was done, with complete success in forty-two and improvement in twelve, and in the thirteen cases of effective pneumothorax thoracocauterization was successful in twelve, with adhesion-free collapse in one and considerable loosening in nine. All types of adhesions were seen. The worst complication, spontaneous pneumothorax due to rupture of the lung, occurred in five, two being fatal. These five, together with four illustrating the value and the limitation of the method and one of unusually grave lung pedicle, are described.

Hemolysis in Pregnancy and Abortion.—Harbitz thinks that in his case, with abortion before admission, there had been a tendency to hemolysis probably due to the pregnancy, and the quinine taken by the patient to induce abortion had increased the hemolysis, which developed into a pure hemoglobinemia and hemoglobinuria, methemoglobinemia and methemoglobinuria, finally causing a fatal uremia. The acute glaucoma with which the disturbance set in and which passed into a panophthalmia is regarded as secondary and ascribed either to increased secretion and changes in the aqueous humor or to action of the quinine directly on the blood vessels. Microscopically, brown and reddish brown masses were seen almost to block the renal canals; there was no glomerulonephritis and but little degeneration of the renal epithelium.

Asymmetrical Sacralization of Fifth Lumbar Vertebra.—Ingebrigtsen sees in his third case of operative asymmetrical sacralization with recovery, here reported, added support for the conception of this disorder as a clinical entity, because the anatomically established sacralization is really the cause of the pain syndrome.

Microsedimentation Reaction with Landau's Pipet.—Frostad says that he found the results of microsedimentation to be as reliable as those of Westergren's sedimentation reaction, while the apparatus and the technic are simpler. The method has many advantages when venipuncture is difficult, especially in pediatrics.